THE MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—43RD YEAR SYDNEY, SATURDAY, SEPTEMBER 29, 1956 No. 13

Table of Contents.

Listerian Oration.[1]

SOME ASPECTS OF RESEARCH INTO VASCULAR DEGENERATION.

By F. R. MAGAREY,

Professor of Pathology, University of Sydney.

THE preparation of an oration such as this is, to me at any rate, a troublesome and time-consuming process, and on the present occasion my chief difficulty has been the choice of subject. With this in mind, I need scarcely remind you that the main reason for this annual function is to honour the memory of Lord Joseph Lister. Lord Lister was a man of many parts, but is most widely remembered because of what was, perhaps, his greatest contribution to the well-being of humanity, the conception and application of the principle of antiseptic technique in surgery. What is less well remembered is that his contributions to scientific knowledge covered a much wider and more fundamental field. Whilst still a house surgeon, Lister performed experiments in which he studied some of the early changes of inflammation; in other words he was an experimental pathologist. He also inquired into the mechanisms of coagulation of the blood, coming to the conclusion that blood is not subject to clotting *in vivo*, unless the inner coat of the blood vessel is injured or diseased. The latter opinion has been refuted in recent years, especially by the work of Duguid, who has shown that small mural thrombi can commonly be demonstrated in otherwise healthy vessels. Duguid has gone a stage further and maintains—not without a considerable weight of evidence—that such repeated mural thrombosis may be the basis of the pathogenesis of atherosclerosis.

In view of these early interests of Lister and following Sir Alexander Murphy's assertion in another context in last year's oration that "atherosclerosis provides a difficult problem", I feel justified in my choice of subject this evening, namely, "Some Aspects of Research into Vascular Degeneration".

In a recent article in THE MEDICAL JOURNAL OF AUSTRALIA I reviewed most of the current theories of the causation of atherosclerosis (or atheroma). In this it was stated that no great future could be foreseen in pursuing further the lipoid and especially the cholesterol hypothesis, for although it is possible to produce lesions in a few animal species by various metabolic insults, seldom do the resultant lesions resemble more than vaguely atheroma as it occurs in the human being. Likewise, there is not much concrete evidence in support of the conception that diet contributes to the pathogenesis of atheroma in man. As Ancell Keys has pointed out, regarding diet and atheroma: "Analysis of mortality from this disease suffers from the inherent weakness of attempting to discover causation from a parallelism between crude estimates of national averages of two variables." Although there appears to be a somewhat closer relationship between the

[1] Delivered at a meeting of the South Australian Branch of the British Medical Association on April 26, 1956.

blood cholesterol level and the formation of atheroma, there is still no definite proof that cholesterol itself gives rise to atheroma. Indeed, in many small (and presumably early) atherosclerotic plaques, although lipoid material is present, it is impossible to demonstrate cholesterol. What right have we, then, to say that cholesterol deposition is the first step in the formation of atheroma?

It is my contention that a more fruitful line of investigation might be to try to show that hypertension makes a direct contribution to the pathogenesis of this disease. It is well known that not only does atheroma increase with age but also, generally speaking, it is more advanced when associated with hypertension. Atheroma is, for instance, much more common in the systemic than in the pulmonary vascular tree, and its frequency in the lung rises sharply in conditions in which pulmonary hypertension develops as in mitral stenosis or generalized emphysema. Likewise, atheromatous plaques are only rarely encountered in veins, although one can usually be found near the origin of the inferior *vena cava*. Venous sclerosis, too, is said to be encouraged by conditions in which there is a chronic rise in the venous blood pressure, as in the portal veins in cirrhosis of the liver.

Working on the hypotheses that, firstly, atheroma is a result of wear and tear of the vessel wall and, secondly, that hypertension acts by accentuating such mechanisms, I have undertaken two lines of investigation which I now propose to describe to you. In case you are labouring under the false impression that a solution to the problem is going to be presented this evening, I must disillusion you at this point and emphasize that the question of pathogenesis still remains unanswered. In other words, I have made no startling new discoveries. These, if any, will have to await the efflux of time.

The first series of experiments in progress have been made possible by a grant from the Life Insurance Medical Research Fund. Lambs are being used in which coarctation of the aorta is surgically induced, the actual operations being performed by Mr. Alan Sharp, without whose help this project could not have been entered upon. It has been undertaken in view of the fact that other observers have frequently commented upon the finding that in coarctation in the human, atheroma is much more advanced in the proximal portion of the aorta than in that part distal to the constriction. The idea is, in other words, to use each animal as its own control.

In spite of early technical troubles, we now have about 20 surviving sheep and, with the use of a capacitance manometer, blood pressure readings from the carotid and femoral arteries indicate that an adequate coarctation has been achieved in many of them.

Surprisingly enough, there is not such a great difference in the proximal and distal mean blood pressures, but the pulse pressure shows a remarkable change. In the normal animal the pulse pressure is higher in the femoral artery than in the carotid, but in our coarctated sheep the position is reversed so that the pulse pressure in the femoral artery is often only a fraction of that in the carotid. If my contention that excessive wear and tear contributes to the formation of atheroma has any substance, then it seems reasonable to hope that we shall succeed in provoking it in the vessels above the coarctation.

So far, no animals have survived for long enough after the creation of the coarctation for us to expect to find arterial degenerative lesions, but I think there are adequate grounds for remaining optimistic, especially as I have been able to find a very occasional focus of lipoid deposition in supposedly normal sheep's aorta obtained from the abattoirs. In other words we do know that sheep are capable of developing lipoid-containing lesions normally.

As an incidental point, our experiments may eventually shed some light on the cause of hypertension in human coarctation. It was once thought that it was a purely hydrodynamic effect, but now general opinion rather suggests that a renal factor also contributes—in much the same way as the ischæmic kidney in the Goldblatt clamp experiments. In some of the coarctated sheep, although the pulse pressure is greatly reduced below the coarctation, the diastolic pressure is actually raised—for example, 145 millimetres of mercury instead of 80 millimetres as in the normal.

Finally, of those animals that have died from extraneous causes, a well-defined post-stenotic dilatation had developed in five cases, in one of these only seven weeks after the coarctation was created.

The second line of research I am going to describe is an investigation into the effects of hypertension on the aorta of the rat. Incidentally, I wanted to ascertain if in this species intimal fibrin deposits occur in a way similar to those demonstrated in the human aorta by Professor Duguid, my erstwhile chief.

Now, the rat is notoriously resistant to the development of experimental atheroma and the naturally occurring disease in this species has to my knowledge only once been rather sketchily recorded. It is not surprising, then, that I have been singularly unsuccessful in shedding any new light on the pathogenesis of atheroma.

Nevertheless, some unusual and hitherto unrecorded changes have been observed, and it is proposed to spend the rest of the time this evening discussing these lesions.

Research into readily produced and reproducible experimental hypertension really began in 1934 with the introduction of what is now known as the Goldblatt clamp. By its use it was shown that partial ischæmia of the kidney may lead to chronic and progressive hypertension.

In 1939 Wilson and Byrom adapted this method for use in the rat, and I have been extremely fortunate in being able to examine the aortas of a considerable number of Dr. Byrom's more recent animals. I am very grateful to him because he has supplied, not only the carcasses, but also the relevant hypertensive history of the individual animals.

The voluminous previous literature has been searched and so far I have been unable to find any reference to changes in the rat's aorta provoked by hypertension. Of course, there are many descriptions of histological changes in smaller vessels, so that it is all the more surprising that there is no comment on the changes I am about to describe.

Two hundred and five rat aortas have been examined, including 81 from normal animals which were taken as controls. The first 50 hypertensives were stained *in toto* with Sudan IV to demonstrate lipoid deposition, but, as all results were negative, this extra manipulation was later abandoned. All the 205 aortas were examined with a dissecting microscope at a magnification of about × 12·5, and by this almost macroscopic means lesions were found in 18, all of which were in the hypertensive group. So that of the 124 hypertensive aortas thus examined 14·5% showed macroscopic lesions. These lesions were usually 0·5 to 2·0 millimetres in diameter and showed as slightly raised, whitish, round or oval plaques. They showed a predilection for the aortic arch, but were not confined to this area, and although in most cases there was only one, in a few there were more and in one case as many as four were found.

Histological examination shows that these plaques consist of cartilage, the smaller ones affecting the intima, and some of the larger the underlying media as well. In some plaques, calcification of the cartilage is a prominent feature. Many frozen sections have been stained to try to detect lipoid, and examined with crossed Nicol prisms to demonstrate cholesterol, but the findings have been consistently negative.

The fact that these cartilaginous lesions were confined to hypertensive aortas, none being found in the normal controls, is, according to my more mathematically minded colleagues, statistically significant. It was therefore decided to make a closer examination in an attempt to determine the pathogenesis of these lesions. To accomplish this, three sections were taken from a representative number of aortas, one from the arch, one from the upper abdominal portion and one just above the bifurcation. These were paraffin embedded and stained usually with hæmatoxylin and eosin.

The normal rat aorta is of very simple construction. The media is made up of eight to 10 regularly alternating layers of elastica and smooth muscle, whilst the intima consists of a single layer of flattened cells closely applied to the medial coat. Only very occasionally are these cells separated from the media by a thin hyaline layer.

Quite striking changes have been found in the aortic intima in many of the hypertensive animals and are essentially of three kinds, namely hyaline deposition, vacuolation and necrosis.

It should be mentioned here that only seldom are changes found in all three sections from the one aorta. This suggests that, had more sections been taken from each vessel, the changes would have been found more frequently. To try to overcome this error in sampling, attempts were made to wind the aorta up like a watch spring and to cut a section in such a way as to include the whole length of the vessel, but this has proved, up till now, to be beyond our technical capabilities.

1. *Hyaline.*—As mentioned before, in the normal animal there may, occasionally, be a very thin hyaline layer between the intima and media. In the hypertensive animals one frequently finds a definite and distinct increase in this hyaline material, which, however, may be quite patchy.

2. *Vacuolation.*—Vacuolation has been observed in the normal aortas only twice, and then in a very mild form. Various degrees have been seen in the hypertensive animals, the more severe grades presenting a very striking picture.

3. *Necrosis.*—In 14 of the hypertensives, but in none of the normal controls, the intimal cells had been replaced by a ragged layer of rather granular, darkly eosinophilic material, in which fragmented remains of nuclei can sometimes be seen. This material bears a striking resemblance to the necrosis seen in arteries in severe hypertension, both in the rat and in the human. This is made even more obvious by the use of Mallory's phosphotungstic acid hæmatoxylin stain. I hope to show later on that this similarity may well be more than coincidence. In one or two specimens, the necrotic change seems to have extended to involve the underlying layer of the media—an observation which will also be referred to later on.

Now that I have demonstrated these various changes, I shall present some figures which suggest that these lesions are, directly or indirectly, the result of hypertension.

Of the 205 aortas, 160 have been examined histologically, 40 from normal and 120 from hypertensive rats, and the findings have been summarized in Table I.

TABLE I.

Group.	Necrosis.	Hyalinization.	Vacuolation.
Normal (40)	0%	12·5%	50%
Hypertensive (120)	11·5%	52·2%	47·5%

I do not think one needs the help of a statistician to be persuaded that, other things being equal, there is a definite relationship between the presence of hypertension and the occurrence of these various intimal changes.

Necrosis was found only in the hypertensives. Further to prove the relationship between hypertension and the other changes, they have been graded according to severity (Table II).

If we take these findings, together with Table I, it can be seen that these changes are not only more common but also more severe in the hypertensive group than in the normotensives.

Dr. Byrom has gone to considerable trouble on my behalf to classify his rats according to the severity of the hypertension from which they suffered. To see if the occurrence of the various lesions just described bears any relationship to the degree of hypertension, the findings have been analysed and are shown in Table III.

Although the numbers involved are too small to satisfy my statistical colleague, Dr. H. O. Lancaster, these figures nevertheless suggest that there is a relationship between the frequency of the lesions and the severity of the hypertension.

TABLE II.

Group.	Normal. (40)	Hypertensive. (120)
Hyaline:		
Slight	10·0%	16·5%
Moderate	2·5% (5)	33·5% (63)
Severe	0%	2·5%
Vacuolation:		
Slight	5·0%	14·0%
Moderate	0% (2)	30·0% (57)
Severe	0%	3·5%

We have now seen that, not only is there some connexion between the occurrence of these changes and the presence of hypertension, but also with the severity of the hypertension—the more severe the hypertension, the more common the lesions.

There is a similar but rather less obvious relationship with the duration of the hypertension, but I do not propose to inflict further figures on you at this stage.

TABLE III.

Degree of Hypertension.	All Cases.	Cartilage.	Necrosis.	Hyaline.	Vacuolation.
±	5·0%	0·0%	0·0%	1·5%	3·5%
+	24·0%	16·5%	21·0%	20·5%	23·0%
++	71·0%	83·5%	79·0%	78·0%	73·5%

I can only postulate upon the sequence and significance of these histological changes and suggest that hyalinization appears first and that vacuolation represents a further degenerative process superimposed.

With regard to necrosis, I have shown you already that the histological appearance of the necrotic intima is very similar to the arterial necrosis characteristic of malignant hypertension in the human.

Many of the hypertensive rats suffered from what Byrom terms cerebral attacks, and he considers that this manifestation indicates either severe hypertension or a rapid rise in the blood pressure. The animals showing such attacks might then be taken as being somewhat analogous to human malignant hypertensives.

If we bear this in mind, and if we can now show that aortic intimal necrosis occurs more frequently in those animals with cerebral attacks than in the group without, then it might be taken as further evidence in support of the suggestion that the two forms of necrosis are at least closely related. Table IV has been constructed to help decide this issue.

Taking all things into consideration, then, it seems reasonable to suggest not only that aortic intimal necrosis is related to severe and rapidly rising blood pressure in the rat, but also that it is similar to the arterial necrosis in human malignant hypertension.

I believe that the cartilaginous plaques I have described represent a form of metaplasia occurring during the healing stages of hyalinization or necrosis. On several occasions it has been possible to observe this change in its very earliest phase. In some sections of necrotic and of hyaline intima, single cells can be found around which there is a condensing halo. Later still the cell with this surrounding structure becomes an unmistakable cartilage cell or group of cells.

As further evidence that cartilage represents a healing stage following intimal degeneration, I must recall the fact that necrosis can occasionally be found affecting not

only the intima but the underlying layer of media as well. If my postulation is correct, one might expect to find cartilage occasionally in the media which in fact is the case, as I have already stated.

TABLE IV.

Group.	All Hypertensives. (120)	Necrosis. (14)
Cerebral attacks not observed ..	38·5%	21·5%
Cerebral attacks observed ..	61·5%	78·5%

Finally, to produce irrefutable proof that these aortic intimal changes are due to hypertension, Mr. Wolfgarten and I are attempting to reproduce them by purely mechanical means.

Byrom and Dodson in 1948 described some experiments in which they forcibly injected saline into rats' arterial systems, thus acutely raising the intravascular pressure. They showed that necrotic arteriolar changes similar to those seen in human malignant hypertension could be produced by this method and postulated that the necrosis was due to the rapid if momentary rise in the intravascular pressure.

As the aortas were not examined in their experiments we are repeating them, paying particular attention to the aortic intimal changes, if any, produced by this manipulation. As a further refinement we are recording the blood pressure in the femoral artery at the time the saline injections are being given into the carotid. A typical tracing shows that the blood pressure rises sharply to a peak of about 250 millimetres of mercury and falls equally rapidly. With the use of two millilitres of saline five or more injections can be given within half a minute, a procedure which one would think must inevitably cause some damage to the vessel walls. That we are near the bursting point of the vessel is indicated by the fact that not uncommonly rats, when sacrificed, are found to have extensive dissecting aortic aneurysms.

Here again I must admit that so far we have been unsuccessful in provoking aortic intimal changes although arterial necrosis has been frequently found. These experiments are also being continued.

I purposely gave this oration a rather vague title, because all I intended to do was describe some aspects of research going on in my department in Sydney.

We do not know where they will lead, but can be moderately certain of one thing—that whatever we find will represent only one tiny piece of the immense and complicated jig-saw puzzle of the pathogenesis of atherosclerosis. It will no doubt remain for others to decide where this piece fits into the general picture of vascular degeneration, if at all.

THE PLURIGLANDULAR SYNDROME, WITH THE REPORT OF A CASE.

By KENNETH F. FAIRLEY,[1] M.D., M.R.A.C.P.

From the Clinical Research Unit of the Royal Melbourne Hospital and the Walter and Eliza Hall Institute of Medical Research, Melbourne.

AFTER Rumpel's work (1896), many Continental authors reported cases of pluriglandular endocrine dystrophy, originally regarded as a primary disease of one gland, usually the thyroid, with secondary depression of function of the others. Claude and Gougerot (1907, 1908) suggested the theory of pluriglandular insufficiency, the various glands being affected by an inflammatory process. Brissaud, Gougerot and Gy (1908) and Gougerot and Gy (1911) reported one such case as tuberculous, but it proved to be the first record of giant-cell granuloma. When Simmonds (1914) described hypopituitarism, it was obvious that most cases of the pluriglandular syndrome were of this type, and the pluriglandular theory was abandoned. The majority of the remaining cases of this syndrome were examples of Addison's disease with secondary hypothyroidism. Sternberg (1914) reported one such case; but Dubois (1919), who described six cases of Addison's disease with chronic lymphoid thyroiditis, gave the first adequate account of this combination. When Schmidt (1926) described two more cases, his name was given to this syndrome. Many cases have now been reported, though in relatively few has the involvement of the thyroid been recognized during life. The clinical features of the adrenal cortical failure often mask the associated hypothyroidism, in the treatment of which great care is necessary, since overdosage with thyroid may precipitate an adrenal crisis, just as it may in cases of hypopituitarism with secondary involvement of the adrenals and thyroid. Crile (1952) reported the successful treatment of chronic lymphoid thyroiditis and of Hashimoto's disease with thyroid and cortisone, and this combination is the obvious therapy for Addison's disease with secondary hypothyroidism.

The reverse condition of primary hypothyroidism with subsequent development of Addison's disease has been far less commonly reported. Paull and Phillips (1954) described one example which clinically and by the various laboratory tests appeared to be a typical case of Addison's disease, except that there was no obvious effect from DCA and cortisone therapy. The hypothyroidism was indicated by the early appearance of intolerance for cold, loss of hair, absence of sweating and the low protein-bound iodine content in the serum of 1·1 microgrammes per 100 millilitres, values below 2·7 microgrammes per 100 millilitres indicating hypothyroidism. The diminution of the follicle-stimulating hormone in the urine below the lower normal level of 6·5 mouse units also suggested a secondary depression of pituitary function. There was a striking clinical improvement on thyroid therapy, with a return to normal values in the results of the Kepler test, in the protein-bound iodine content of the serum, in the basal metabolic rate, and in the eosinophile cell and 17-ketosteroid response to ACTH, although it took nine months for the adrenal function to recover fully.

The literature on pluriglandular insufficiency was very fully reviewed by Rickards and Barrett (1954), who reported three cases of Addison's disease, the first due to, and the second possibly an example of, giant-cell granuloma, a specific condition often manifesting itself as hypopituitarism (Rickards and Harvey, 1954). Lesions have been reported in the pituitary, adrenals, testes, liver and spleen, and in vascular tissue. The first and second patients presented clinically as examples of Addison's disease with hypothyroidism, and all three showed varying degrees of chronic lymphoid thyroiditis with atrophy of the acini. They suggest that giant-cell granuloma should be suspected when hypopituitarism occurs with no history of post-partum hæmorrhage or collapse, and when tumour, tuberculosis and syphilis have been excluded. At autopsies on subjects of non-tuberculous Addison's disease or hypopituitarism, a careful search for such granulomata should be made.

In the patient whose history follows the Addison's disease was presumably non-tuberculous in origin, for no evidence of tuberculosis could be found. There were associated hypothyroidism and ovarian deficiency, but, in the absence of facilities for estimation of follicle-stimulating hormone values, it was impossible to determine whether the ovarian deficiency was a primary ovarian defect or was secondary to a deficiency in gonadotrophin secretion. The underlying pathological background is unknown, but the condition certainly was not primary hypopituitarism. Ultimately it may prove to be an example of a giant-cell granuloma; but in any case, it is apparently a rare condition.

[1] Drug Houses of Australia Fellow.

Report of a Case.

Mrs. T., aged twenty-eight years, was admitted to the Royal Melbourne Hospital under the care of Dr. Pincus Taft on July 29, 1954. There was nothing of note in the family history. When the patient was aged eight years a subtotal thyroidectomy had been performed for a diffuse toxic goitre. Considerable exophthalmos persisted until about the age of eighteen years, when it gradually decreased. At this time there developed a greatly increased sensitivity to cold, a craving for salt (eaten with lemon), and seasonal urticaria affecting the lips. Three years later the urticaria was replaced by hay fever, which became progressively more troublesome. Intermittent treatment with thyroid was given without much benefit.

For nine months after her marriage at the age of twenty-three years the patient's libido was normal. Then one month before her only pregnancy commenced, nausea, lassitude and undue fatigue appeared. Throughout pregnancy, nausea and vomiting persisted, and she had never felt well since. Labour was uneventful, without undue hæmorrhage. For the next month hot flushes were frequent. At the age of six weeks the baby was weaned because of inadequate milk supply, and the breasts involuted normally. During the pregnancy the areolæ and nipples had become normally pigmented, and the pubic hair was normal. The patient did not know when the pigmentation of the areolæ disappeared or when the pubic hair became sparse. Regular painless menstruation, lasting four to five days and with considerably diminished loss, recommenced two months after childbirth. Formerly the menses, which had begun at the age of eleven years, had been painful and excessive and had lasted for seven to eight days.

For the next four years preceding her admission to hospital, the patient's main symptoms were undue fatigue, irritability, lassitude, complete loss of libido, brief faint feelings without loss of consciousness, increased sensitivity to cold, and poor memory. This last symptom made it difficult to obtain an accurate history, especially in regard to time relationships.

Three years prior to her admission to hospital, treatment with thiouracil proved valueless. Amenorrhœa developed suddenly one year later, and rheumatic pains in the neck appeared. Increasing pigmentation was first noticed seven months prior to her admission to hospital. Three months later cortisone, given for a month, led to a decrease of the pigmentation; this again increased after the drug was omitted. On May 15, 1954, 600 milligrammes of DCA were implanted, and despite this relatively large dose, the craving for salt returned after a month. During the withdrawal of cortisone the dose was suddenly reduced from 75 milligrammes to 25 milligrammes per day. On that night severe generalized joint pains prevented sleep, and subsequently intermittent arthralgia became troublesome. The only other symptoms of note were nocturnal frequency of micturition and the loss of one and a half stone in weight in the previous two years.

Examination of the patient revealed a very slight exophthalmos, with lid lag and some swelling of the lower eyelids. A small nodule of thyroid tissue (two by one centimetre in area) was present in the left side of the neck. Generalized increased brownish pigmentation of the skin was present with involvement of the buccal mucosa, but there was a striking lack of pigmentation of the areolæ and nipples, and no pigment was present on the vulva or vaginal mucosa. The pubic and axillary hair was very sparse. The uterus was a little smaller than normal, and no specimen could be obtained on attempted endometrial biopsy. The pulse rate was 70 per minute and the blood pressure was 140 millimetres of mercury, systolic, and 90 millimetres, diastolic. Some four months previously, before any cortisone and DCA had been given, the blood pressure was 100 millimetres of mercury, systolic, and 60 millimetres, diastolic. The fundi and visual fields were normal. The urine was free from albumin and sugar, contained 13 grammes of chloride per litre, and was normal on microscopic examination. Renal function tests gave normal results.

Several complete blood examinations gave approximately normal findings during the patient's various admissions to hospital. The leucocytes varied in number from 5000 to 8000 per cubic millimetre, and eosinophile cells were present in normal numbers. The blood sedimentation rate was somewhat increased and slowly returned to normal over the next few months. The results of the Wassermann and Kahn tests on the blood and the Mantoux test (1 in 100) were negative. No tubercle bacilli were found in the sputum. Radiological examination of the heart, lungs, skull, *sella turcica* and adrenal areas revealed no abnormality.

The basal metabolic rate was estimated on August 2, 1954, as +10%, on October 15, 1954, as −17%, and on March 10, 1955, as +14%. The blood cholesterol content was 190 milligrammes per 100 millilitres, and the total fasting blood lipid content was 975 per 100 millilitres. On August 17 and 24, 1954, the protein-bound iodine levels were 1·7 and 1·4 microgrammes per 100 millilitres respectively, low values compatible with myxœdema. The electrocardiogram showed inverted *T* waves and a prolonged *Q-T* interval (0·44 second). After potassium chloride had been taken for four days the *T* waves were upright. After some two months of treatment with cortisone, testosterone and thyroid, the *Q-T* interval was at the upper limit of normal, but after the patient had been off thyroid for one month it was again prolonged.

The alkali reserve and plasma chloride content were approximately normal, and the first part of the Kepler test showed a delay in water excretion. The fasting blood sugar content was invariably at hypoglycæmic levels, ranging from 36 to 56 milligrammes per 100 millilitres in five tests between July and October, 1954. The glucose tolerance curves were flat, the highest level reached in three tests being 112 milligrammes, and after the subsequent fall hypoglycæmic levels were maintained throughout the tests.

No appreciable reduction in eosinophile leucocytes followed either the injection of adrenaline or an intravenous infusion of 25 milligrammes of ACTH given over eight hours. Likewise there was no response to the daily administration of ACTH from August 9 to August 14, 1954, as judged by the eosinophile cell count and the excretion of 17-ketosteroids. For the first three days 20 milligrammes of long-acting ACTH[1] were given intramuscularly twice a day, and for the last two days 40 milligrammes of ACTH were given per day in two litres of normal saline by continuous intravenous infusion. At noon on August 13 the patient rapidly went into hypoglycæmic coma, which responded dramatically to 20 millilitres of a 50% solution of glucose given intravenously. Cortisone, 50 milligrammes, was given intramuscularly at once. Next morning the intravenous infusion was stopped and cortisone was given orally, 50 milligrammes per day for two days and then 37·5 milligrammes per day, along with potassium citrate, 90 grains per day.

The adverse effect of ACTH was striking. On the first day it was given, weakness and nausea were noticed, and for the next three days nausea and vomiting were present. After the hypoglycæmic coma headache was severe, and next day drowsiness, diarrhœa and vomiting were troublesome, and puffiness of face and œdema of the legs appeared. The weight, previously steady, had increased by five pounds in the five days of ACTH therapy, which was then discontinued. In the next two days, despite cortisone therapy, there was a loss of eight pounds in weight accompanied by a copious diuresis and a very much lowered concentration (1% to 2%) of chloride in the urine. For five days after ACTH was omitted, visual and auditory hallucinations were present, but the vomiting slowly subsided and thereafter the patient's condition improved steadily. Professor E. B. Astwood, of Boston, in a personal communication, stated that he had seen a hypoglycæmic coma apparently precipitated by the use of ACTH in a patient with Addison's disease.

By the use of frog's skin, the presence of a melanophore-expanding substance was demonstrated in the blood. This is almost certainly the melanocyte-stimulating hormone.

The patient left hospital on August 31, 1954, taking daily cortisone, 37·5 milligrammes orally, and methyl testosterone, 10 milligrammes sublingually, and was readmitted to hospital on October 13. Two weeks after she had left hospital a sudden improvement had occurred, with increased appetite and energy, diminished irritability, better tolerance for cold and ability to do normal work without undue fatigue. However, libido remained absent. She had gained one stone in weight. The blood pressure was 160 millimetres of mercury, systolic, and 90 millimetres, diastolic. Pigmentation had decreased considerably and the thyroid nodule had completely disappeared.

The uptake of I^{131} by the thyroid at three hours was 33·5%, a value much higher than the normal. The protein-bound iodine content had risen to 3·4 microgrammes per 100 millilitres, a decided increase from the hypothyroid values present two months before. Two millilitres of "Ambinon" (a thyroid-stimulating hormone preparation manufactured by Organon Laboratories) were given, and twenty-four hours later the three-hour uptake after another tracer dose of I^{131} was unaltered (33·7%), but the protein-bound iodine

[1] The ACTH used was manufactured by the Commonwealth Serum Laboratories of Australia and contained four units of "Pitressin" per 100 milligrammes of ACTH.

content had risen to 4·5 microgrammes per 100 millilitres. The protein-bound iodine was determined as the average of three estimations in duplicate to ensure that the result was satisfactory, hence the rise of 1·1 microgrammes was significant. The Kepler test showed practically equal volumes for the night and day specimens, and the calculated index of 24 indicated a positive result for Addison's disease, although the last dose of cortisone had been given only four hours before the commencement of collection of the night urine.

The patient left hospital on October 19, taking the same dose of cortisone and methyl testosterone, with the addition or half a grain of thyroid for two weeks, the dose being then increased to one grain daily; the intermittent use of 0·5 milligramme of stilbœstrol per day for three weeks in each month was instituted. When the patient was reviewed again from December 29 to 31 her only complaint was a daily headache. Three scanty vaginal hæmorrhages had occurred, but these did not correspond with periods of œstrogen withdrawal. Libido had returned, and her general health was better than it had been since her pregnancy five years before. She was still unduly sensitive to cold, so the dose of thyroid was gradually increased to three grains per day, and stilbœstrol was omitted. The pulse rate was 76 per minute, the blood pressure was 150 millimetres of mercury, systolic, and 80 millimetres, diastolic, and there was a general decrease in pigmentation, except for a slight increase in pigmentation of the areolæ. The axillary and pubic hair, though still rather sparse, had increased appreciably. The serum cholesterol content was 260 milligrammes per 100 millilitres, the fasting blood sugar content had risen to 90 milligrammes per 100 millilitres, and the serum sodium and potassium values were within normal limits.

When the patient was readmitted to hospital for review from March 7 to 17, 1955, she had gained a stone in weight, and her health had been fairly good until the discontinuation of methyl testosterone and thyroid one month previously, cortisone having been the only medication taken over the last month. Within a week of the omission of these hormones, there was loss of libido to the extent that she had a revulsion to intercourse, a state identical with that present on her first admission to hospital. There was a gradual onset of loss of energy, fatigue, depression, irritability, anorexia and very greatly increased sensitivity to cold. Aching developed in the head, neck and right forearm. The memory was poor and the eyes were puffy in the morning. The areas of vitiligo had disappeared and pigmentation had returned to normal, save that there was no pigmentation of the areolæ. The facies was typical of hypothyroidism, and the blood pressure was 130 millimetres of mercury, systolic, and 70 millimetres, diastolic.

The blood picture and the serum sodium and potassium values were normal. Five minutes after the intravenous injection of 18 grammes of glucose, the blood sugar had risen from the fasting level of 56 to 240 milligrammes per 100 millilitres, and subsequent values at half-hourly intervals were 144, 50, 26, 52, 56 and 50 milligrammes per 100 millilitres. This pronounced reactive hypoglycæmia ninety minutes after injection is found in about half the patients with Addison's disease. There was also a slight "glucose fever" nine hours after the test, a not uncommon occurrence in this disease.

The serum cholesterol content had risen to 400 milligrammes per 100 millilitres and the total lipides to 1000 milligrammes per 100 millilitres on March 8. The uptake of I^{131} at three hours was 33%. The protein-bound iodine content had risen to 5·8 migrogrammes per 100 millilitres. After two millilitres of "Ambinon" had been injected twice a day to a total of 10 millilitres, the uptake of I^{131} at three hours was 32% and the protein-bound iodine content was 6·6 microgrammes per 100 millilitres (Figure I). These results were similar to those obtained in October, 1954, except for the higher level of the protein-bound iodine before thyroid-stimulating hormone was given, this rise presumably being due to cortisone therapy. The amount of compound F in the serum was 4·1 microgrammes per 100 millilitres; after the intramuscular administration of long-acting ACTH, 20 milligrammes twice a day for six days, the amount was 3·8 microgrammes per 100 millilitres; these values are in the lower range of normal (Figure I). In each instance they were estimated forty-eight hours after the cessation of cortisone therapy, maintenance doses of which were given for the first four days of the test because of the toxic effects encountered when ACTH was given previously. There was no change in the excretion of 17-ketosteroids under these conditions (Figure I). The adrenal glands were obviously unresponsive to ACTH stimulation.

The patient left hospital on March 17, 1955, being maintained on a daily dosage of 25 milligrammes of cortisone, 10 milligrammes of methyl testosterone and one grain of thyroid; the dosage of thyroid was increased gradually to three grains per day. On May 16 her memory was still poor and libido was absent. A recent episode of giant urticaria lasting one day had been followed two days later by hay fever. Pains in the knees and hands, worst in the morning and relieved by exercise, had been present for two months, and pain in the right costo-vertebral angle had been noted for one month. For a fortnight hot flushes had occurred with hot sweating hands, and she had lost the undue sensitivity to cold. The daily dose of three grains of thyroid appeared to be the correct amount to abolish the symptoms of hypothyroidism. She had undoubtedly felt better when taking a small dose of stilbœstrol in addition to these other hormones.

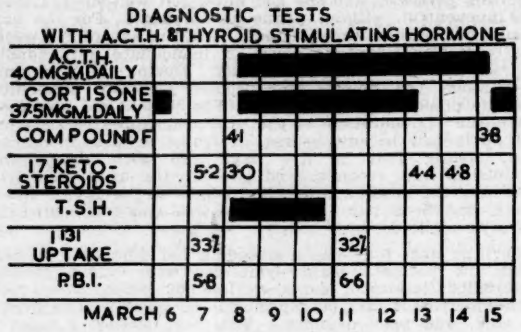

FIGURE I.

Illustrating the lack of response of the adrenal glands to stimulation with ACTH and the insignificant response of the thyroid gland to thyroid-stimulating hormone. (Five months earlier a slight but significant rise of 1·1 microgrammes per 100 millilitres in the protein-bound iodine level had followed a single injection of two millilitres of "Ambinon".) Compound F and protein-bound iodine are recorded as microgrammes per 100 millilitres of serum and 17-ketosteroids as milligrammes per twenty-four hour output of urine. The dosage of thyroid-stimulating hormone was two millilitres of "Ambinon" twice a day to a total of 10 millilitres. The I^{131} uptake was estimated three hours after the tracer dose had been given.

Discussion.

Adrenal Cortical Failure.

This patient showed evidence of deficient function of several endocrine glands, but unlike most of these cases the primary failure was not in the anterior pituitary lobe. There is definite evidence of a primary failure of the adrenal cortex. The craving for salt and the low blood pressure both relieved by DCA, the pigmentation, the loss of pubic and axillary hair, the results of intravenous and oral glucose tolerance tests, and the hypoglycæmic coma were typical of Addison's disease. The very good therapeutic response to cortisone and the failure to respond to the prolonged use of ACTH (shown clinically by the development of hypoglycæmic coma, and in the laboratory by the unchanged eosinophile count, the excretion of 17-ketosteroids and the amount of compound F in the serum) indicate that the failure of the adrenal cortex was primary and not secondary to the lack of ACTH.

That the coma which developed during the test with ACTH was hypoglycæmic in origin was proved by the dramatic response to an intravenous injection of glucose. In hypopituitarism, coma may arise from various causes, including water intoxication. Whittaker and Whitehead (1954) record a case of hypopituitarism in which the patient, while on ACTH therapy, twice went into coma, apparently owing to water intoxication related to the pitressin content of the particular ACTH used. Similarly in this patient with Addison's disease and hypothyroidism there was difficulty in the excretion of water, and perhaps she was more sensitive than normal to the antidiuretic effect of pitressin. The rapid gain in weight while she

was receiving ACTH (which contained four units of pitressin per 100 milligrammes) and the even more rapid loss of weight with a copious diuresis, despite the use of cortisone, in the two days after ACTH therapy was discontinued, indicate that considerable retention of fluid occurred in the five days of the test. Over this period anorexia, nausea, vomiting, headache and visual and auditory hallucinations became prominent and were consistent with the development of water intoxication.

Hypothyroidism.

Hill *et alii* (1950) found that most subjects with Addison's disease had a normal uptake of I^{131} by the thyroid and normal protein-bound iodine levels in the serum. In some cases cortisone, in relatively large doses of 50 to 100 milligrammes per day, temporarily increased the iodine uptake, which returned to normal or subnormal values on continued administration, whilst the protein-bound iodine content tended to decrease slightly. Cortisone in smaller doses of 10 to 20 milligrammes per day led to a variable thyroid response in Addison's disease. Implants of pellets equivalent to a dose of 10 milligrammes of cortisone per day had no consistent effect on I^{131} uptake or protein-bound iodine content. Since thyroid-stimulating hormone overcame the inhibition of thyroid function induced by cortisone in normal subjects, these workers considered that adrenal steroids suppressed thyroid activity indirectly through inhibition of the pituitary gland.

That this patient suffered from hypothyroidism was shown clinically by lassitude, undue sensitivity to cold, poor memory and characteristic facies; it was confirmed by the high serum cholesterol content, the low initial protein-bound iodine level in the serum and the response to thyroid therapy. It is of interest that the earliest symptoms of hypothyroidism appeared about the same time as the first symptom (salt craving) of what later proved to be Addison's disease, and when the exophthalmos, which had persisted for ten years after thyroidectomy, began to subside. If the exophthalmos is related to excessive secretion of exophthalmic factor and the accompanying thyroid-stimulating hormone, a diminution of such secretion would lead to reduction in exophthalmos and a lessened stimulation of the post-operative thyroid remnant, which might not then be able to maintain the patient in a euthyroid state. However, the disappearance of the moderate-sized nodule of thyroid tissue and the considerable increase in protein-bound iodine under cortisone therapy indicated that the hypothyroidism was most closely related to the adrenal cortical deficiency. The high retention of I^{131} at three hours in the initial test (33%) and the low normal level of protein-bound iodine (3·4 microgrammes per 100 millilitres) were compatible with the post-operative reduction in thyroid tissue, the small thyroid remnant working overtime in the attempt to provide sufficient thyroid hormone. These results might indicate an impaired ability of the gland to transfer inorganic iodine to organic compounds. Unfortunately the retention of radio-iodine was not investigated until after cortisone had been given for two months.

On two occasions a slight rise in protein-bound iodine level (1·1 and 0·8 microgramme per 100 millilitres respectively) followed the administration of thyroid-stimulating hormone after the patient had been receiving 37·5 milligrammes of cortisone daily, with a rise in the protein-bound iodine level over two months from 1·7 to 3·4 microgrammes per 100 millilitres, and after another five months to 5·8 microgrammes per 100 millilitres, though thyroid had also been given for the first four of these last five months. This very appreciable rise in the protein-bound iodine in response to cortisone suggests that the relatively small rise in the protein-bound iodine after thyroid-stimulating hormone was not due solely to the post-operative reduction of thyroid tissue, but also to damage to the gland from the most important ætiological factor in the hypothyroidism, the lack of adrenal cortical hormones, which probably resulted in chronic lymphoid thyroiditis. The post-operative reduction in the amount of thyroid tissue would necessarily diminish the functional reserve of the gland and so facilitate the production of a hypothyroid state by anything which further reduced the function of the gland. Jefferies *et alii* (1953) showed that some patients with a low thyroid reserve, usually due to previous subtotal thyroidectomy or I^{131} therapy, had normal initial uptake and protein-bound iodine values even when mild hypothyroidism was present; but these patients showed a poor response to stimulation with thyroid-stimulating hormone, as indicated by a smaller rise than normal in both uptake and protein-bound iodine levels. This suggests that the remnant of the gland is already functioning near to its maximum in response to endogenous thyroid-stimulating hormone. Two tests in the present case gave results of this type, save that the initial uptake was much higher than normal. The patient's thyroid gland had already benefited by cortisone therapy for two months before the first test.

As was mentioned previously, cases of Addison's disease supervening on hypothyroidism have been reported comparatively rarely. In myxœdema, failure of the adrenal cortex may be mediated through the pituitary gland, or it may be due to a direct effect on the adrenal cortex of the lack of thyroid hormone. A low urinary excretion of 17-ketosteroids is usual in myxœdema, and they increase if adequate thyroid therapy is given (Kenigsberg and McGavack, 1954). Failure of ACTH production in myxœdema is well authenticated (Garrod and Gilliland, 1954). A delayed response to ACTH may occur in myxœdema, and indicates a direct depression of the adrenal cortex. Confusion in the interpretation of results may arise if ACTH stimulation is not continued long enough to elicit a response. In the present case, on two occasions ACTH was given for five to six days, once before thyroid therapy was instituted, and again one month after thyroid was omitted after four months of treatment. The failure to respond to ACTH on both occasions indicates that the adrenal cortical failure was certainly not mediated through the pituitary, either from a primary pituitary lesion or from primary hypothyroidism with secondary depression of pituitary function.

Ovarian Deficiency.

Amenorrhœa is uncommon in uncomplicated Addison's disease, and in hypothyroidism menorrhagia or *metropathia hæmorrhagica* is usual, while amenorrhœa is much less common. The sudden onset of amenorrhœa two years previously in this young woman, who had always menstruated regularly before and after her pregnancy and who was still in moderately good health, is suggestive of failure at the hypothalamic-pituitary level with secondary ovarian deficiency. A primary ovarian failure in such a case usually results in a gradual disappearance of the menses, hypomenorrhœa and oligomenorrhœa preceding the amenorrhœa.

A very similar history was recorded by Crispell and Parson (1952), that of a patient with *diabetes mellitus*, Addison's disease, myxœdema, amenorrhœa, and a lack of pigmentation of nipples and areolæ. The excretion of follicle-stimulating hormone was normal. At autopsy the pituitary gland was normal, and the ovaries on microscopic examination had multiple follicular cysts, but no *corpus luteum* was present.

Most striking in the present case was the absence of any pigmentation of the nipples and areolæ, areas which in typical Addison's disease are intensely pigmented. The vulva and vagina also showed no increased pigmentation. There is evidence that such lack of pigmentation indicates ovarian deficiency. Lipschutz (1930) found that in castrated male guinea-pigs, transplantation of an ovary was followed by pigmentation of nipples and areolæ. Œstrogen applied locally (Wheeler *et alii*, 1953) or given internally produced similar pigmentation in castrated male guinea-pigs (Bloch and Schrafl, 1932). In young females with defective ovarian function, particularly in those with ovarian hypoplasia or aplasia, who are treated with fairly large doses of œstrogen, very deep pigmentation of the nipples and areolæ may result and a pronounced *linea nigra* may develop (Davis *et alii*, 1945). The increased pigmentation of these areas in pregnancy may be related to more than one factor.

The increased pigmentation in Addison's disease is thought to be due to excessive secretion of melanocyte-stimulating hormone by an intact intermediate lobe of the pituitary. Normally this hormone is antagonized by the adrenal cortical hormones, and the high level of melanocyte-stimulating hormone in Addison's disease is lowered when cortisone is given (Schizume *et alii*, 1954). This increased pigmentation may disappear with cortisone therapy.

In Simmonds's disease, and in hypopituitarism from most other causes, there is a characteristic loss of pigmentation. Here the intermediate lobe presumably is involved, with interference with the production of melanocyte-stimulating hormone. However, Steinberg, Schechter and Segal (1954) report a case of "pituitary Addison's disease", in which there was a selective failure of ACTH production and pigmentation was increased. The secretion of melanocyte-stimulating hormone was presumably unaffected, but there was secondary adrenal cortical failure. Lerner, Schizume and Bunding (1954) produced pigmentary changes typical of Addison's disease by giving large doses of purified melanocyte-stimulating hormone to normal adults. They report the history of one patient, maintained on 50 milligrammes of cortisone daily after the radical removal of one breast, both ovaries and both adrenal glands, who was given large doses of melanocyte-stimulating hormone. Despite the relatively large dose of cortisone, she developed widespread pigmentation of the body with new black nævi on the face and arms, but the areola did not become pigmented. The ovaries are intimately related to pigmentation of the areolæ (probably an œstrogen effect), and lack of increased pigmentation in these areas in a patient subjected to an excess of melanocyte-stimulating hormone, exogenous (experimentally) or endogenous (Addison's disease), is an indication of ovarian deficiency. This might be used as a test of ovarian function with regard to the production of œstrogens. It is of interest to note that in the present patient, the addition of testosterone to cortisone therapy resulted in a loss of revulsion to intercourse; but it was not until œstrogen was also added that a definite return of libido was apparent. Since facilities for the estimation of F.S.H. were not available, it was impossible to determine whether the ovarian deficiency was secondary to lack of gonadotrophins or due to a primary ovarian disorder.

There is evidence of deficient hormone production by several ductless glands in this patient, but the ætiology and underlying pathology are as yet unknown.

Summary.

1. In the pluriglandular syndrome, there is inadequate production of hormones by several ductless glands, the clinical picture having many resemblances to that of anterior pituitary deficiency. Many of these patients suffer from a combination of primary Addison's disease with secondary hypothyroidism due to chronic lymphoid thyroiditis.

2. The history is reported of a female patient, aged twenty-eight years, who presented with this syndrome. She was treated surgically at the age of eight years for exophthalmic goitre, and twenty years later had evidence of deficient hormone production by the adrenal and thyroid glands and the ovaries.

3. Primary adrenal deficiency was shown by the typical clinical picture of primary Addison's disease, the therapeutic response to cortisone and the complete failure to respond to ACTH, the use of which precipitated hypoglycæmic coma.

4. Hypothyroidism was shown by the characteristic symptoms and facies, the high serum cholesterol level, the low initial protein-bound iodine values and the response to thyroid therapy. The appreciable rise in the protein-bound iodine with cortisone therapy alone (from 1·7 to 3·4 microgrammes per 100 millilitres) and the disappearance of the thyroid nodule on this therapy indicated that the hypothyroidism was, in large part, secondary to the adrenal cortical failure. The loss of thyroid tissue at operation had, of course, lowered the thyroid reserve.

5. Ovarian deficiency was suggested by the sudden onset of amenorrhœa in a young woman who had always menstruated regularly before and after her pregnancy, and who was at the time still in moderately good health. The striking lack of pigmentation of the nipples and areolæ in this case of primary Addison's disease is considered to be reliable evidence of ovarian failure, particularly with regard to the production of œstrogens.

6. Of the several therapeutic regimes prescribed, the greatest general benefit was obtained from the combination of daily doses of 37·5 milligrammes of cortisone and 180 milligrammes of dried thyroid taken orally with 10 milligrammes of methyl testosterone taken sublingually, while the daily addition of 0·5 milligramme of stilbœstrol by mouth for three weeks in every month was necessary to restore her libido to normal.

Acknowledgements.

My thanks are due to Dr. Pincus Taft for his continual help and for permission to publish this case history, and to Mrs. D. Winikoff, Miss S. Weiden, Dr. J. Bornstein and Dr. B. Hudson for their unstinted assistance with the biochemical investigations.

References.

BLOCH, B., and SCHRAFL, A. (1932), *"Experimentelle Untersuchungen über den Einfluss des Ovarialhormons auf die Pigmentbildung", Arch. f. Dermat. u. Syph.*, 165: 268.

BRISSAUD, E., GOUGEROT, H., and GY, A. (1908), *"Insuffisance endocrinienne thyroïdotesticulaire", Rev. neurol.*, 16: 1354.

CLAUDE, H., and GOUGEROT, H. (1907), *"Sur l'insuffisance simultanée de plusieurs glandes à sécrétion interne. (Insuffisance pluriglandulaire)", Mém. Soc. biol.*, 11: 785.

CLAUDE, H., and GOUGEROT, H. (1908), *"Les syndromes d'insuffisance pluriglandulaire. (Leur place en nosographie)", Rev. med.*, 28: 861, 950.

CRILE, G., junior (1952), "Thyroiditis", *Ann. Int. Med.*, 37: 519.

CRISPELL, K. R., and PARSON, W. (1952), "Administration of Purified Growth Hormone to a Female with Hypoadrenalism, Hypothyroidism, Diabetes Mellitus and Secondary Amenorrhœa, Simulating Panhypopituitarism", *J. Clin. Endocrinol.*, 12: 881.

DAVIS, M. E., BOYNTON, M. W., FERGUSON, J. H., and ROTHMAN, S. (1945), "Studies on Pigmentation of Endocrine Origin", *J. Clin Endocrinol*, 5: 138.

DUBOIS, M. (1919), *"Ueber das Vorkommen lymphatischer Herde in der Schilddrüse bei Morbus Addisonii", Berl. klin. Wchnschr.*, 56: 1178.

GARROD, D., and GILLILAND, I. E. (1954), discussion on hypothyroidism, *Proc. Roy. Soc. Med.*, 47: 885.

GORDON, D., HORWITT, B. N., and SEGALOFF, A. (1954), "Adrenal Response to A.C.T.H. in Various Clinical Conditions", *J. Clin. Endocrinol.*, 14: 297.

GOUGEROT, H., and GY, A. (1911), *"Insuffisance pluriglandulaire interne thyro-testiculo-surrénale. Nouvelle observation clinique et anatomique", Nouv. iconog. de la Salpêt.*, 24: 449.

HILL, S. R., junior, REISS, R. S., FORSHAM, P. H., and THORN, G. W. (1950), "The Effect of Adrenocorticotrophin and Cortisone on Thyroid Function: Thyroid-Adrenocortical Relationships", *J. Clin. Endocrinol*, 10: 1375.

JEFFERIES, W. McK., LEVY, R. P., PALMER, W. G., STORAASLI, J. P., and KELLY, L. W. (1953), "The Value of a Single Injection of Thyrotropin in the Diagnosis of Obscure Hypothyroidism", *New Eng. J. Med.*, 249: 876.

KENIGSBERG, S., and MCGAVACK, T. H. (1954), "17 Ketosteroid and Pituitary Follicle Stimulating Hormone Excretion in Myxœdema Before and After Treatment with Thyroxine", *J. Clin Endocrinol*, 14: 929.

LERNER, A. B., SHIZUME, K., and BUNDING, I. (1954), "Mechanism of Endocrine Control of Melanin Pigmentation", *J. Clin. Endocrinol.*, 14: 1463.

LIPSCHÜTZ, A. (1930), *"Über den Ort der Pigmentbildung", Virchows Arch. f. path. Anat.*, 276: 676.

PAULL, A. M., and PHILLIPS, R. W. (1954), "Primary Myxœdema with Secondary Adrenal Cortical Failure", *J. Clin. Endocrinol*, 14: 554.

RICKARDS, A. G., and BARRETT, G. M. (1954), "Non-tuberculous Addison's Disease and its Relationship to 'Giant-Cell Granuloma' and Multiple Glandular Disease", *Quart. J. Med.*, 23: 403.

RICKARDS, A. G., and HARVEY, P. W. (1954), "'Giant-Cell Granuloma' and the Other Pituitary Granulomata", *Quart. J. Med.*, 23: 425.

RUMPEL (1896), *Neurol. Centralbl.*, 15: 428.

SCHMIDT, M. B. (1926), *"Eine biglanduläre Erkrankung (Nebennieren und Schilddrüse) bei Morbus Addisonii", Verhandl. deutsch. pathol. Gesellsch.*, 21: 212.

SHIZUME, K., and LERNER, A. B. (1954), "The Determination of Menalocyte-stimulating Hormone in Urine and Blood", *J. Clin. Endocrinol.*, 14: 1491.

SIMMONDS, M. (1914), *"Ueber Hypophysisschwund mit tödlichem Ausgang", Deutsch med. Wchnschr.*, 40: 322.

STEINBERG, A., SCHECHTER, F. R., and SEGAL, H. I. (1954), "True Pituitary Addison's Disease: A Pituitary Unitropic Deficiency", *J. Clin. Endocrinol.*, 14: 1519.

STERNBERG, H. (1914), *Verhandl. deutsch pathol Gesellsch.*, 17: 233.

WHEELER, C. E., CAWLEY, E. P., and CURTIS, A. P. (1953), "Effects of Topically Applied Hormones on Growth, Pigmentation and Keratinization of Nipples and Areolæ", *J. Invest. Dermat.*, 20: 385.

WHITTAKER, S. R. F., and WHITEHEAD, T. P. (1954), "The Diagnosis and Treatment of Hypopituitarism", *Brit. M. J.*, 2: 265.

SOME ASPECTS OF PULMONARY TUBERCULOSIS IN THE AGED.

By W. BOLLIGER,
Heatherton Sanatorium, Melbourne.

THIS study has been based on patients, aged seventy years and over, on their admission to the three major Victorian sanatoria over the past two years. It has long been known that those of advanced years may present with, though not necessarily be suffering from, pulmonary tuberculosis; it has perhaps not been so widely recognized. Of recent years increasing attention has been focused on the aged. This attention derives from the fact that the expectation of life has gone up, and that the aged are more plentiful. A host of important economic, social and medical problems have ensued, and the proportion of the national revenue which could or should be set aside for the aged is widely discussed.

In Victoria the annual number of notified new cases of tuberculosis covering all age groups has in recent years not declined. Nevertheless the number of patients considered to require sanatorium treatment has diminished. Because of this, and because of a quicker turnover of patients, waiting lists for admission have sharply decreased. Beds, especially for males, are freely available. The prompt admission to sanatoria of the aged with tuberculosis is now possible in Victoria. In fact, compared with other chronic illnesses in the aged, it is easier for a practitioner to obtain a bed if pulmonary tuberculosis, however mild, can be diagnosed. Knowledge of this fact has on occasions been misused to gain admission for an elderly "chronic" under the guise of "emergency". Once admitted, the aged tend to stay on because they have nowhere suitable to live, or because they are too feeble from other causes to exist outside. Aged patients are hence becoming increasingly numerous in sanatoria.

In the community in general aged women predominate over males, but among the tuberculous aged the ratio of men to women is about six to one. Females with tuberculosis tend to die at earlier ages. (See Table I.)

The financial position of the group under discussion is as follows. Whilst in a sanatorium an unmarried male patient receives £4 a week (tuberculosis allowance) in addition to board, lodging and treatment. After his discharge the tuberculosis allowance, which continues for a variable period, amounts to £6 2s. 6d. (almost half the basic wage).

On the other hand, the old-age pension for an unmarried male amounts to £4 a week (about one-third of the basic wage). On this he has to feed, clothe and house himself, unless he is able to work and is fortunate enough to find suitable employment. Under such circumstances he is permitted to earn an additional £3 10s. per week.

Circumstances Preceding Admission to a Sanatorium.

Patients may arrive at a sanatorium as a sequel to one or more of the following events: (i) hæmoptysis; (ii) respiratory tract infection; (iii) investigation for some other illness, such as cardio-vascular or prostatic disease; (iv) persistent cough and sputum; (v) tracing of contacts. Few of the aged tuberculous have reached a sanatorium as a result of the tracing of contacts; they have been found as a result of symptoms and signs which they themselves exhibit. Some on being questioned may reveal the history of a sibling or of a child who died of tuberculosis twenty and more years ago. When one is investigating a family for possible tuberculosis, it may be difficult to persuade the aged to come for an X-ray examination. Their attitude is that, having survived to an advanced age, they must therefore be healthy. In their terminal illness the sputum may be found to contain tubercle bacilli, and the aged member of the household is shown to have been not so innocuous after all.

The history and the X-ray findings usually indicate that the infection is of long standing, with some recent changes. The time lag between the onset of significant symptoms and adequate investigation is much greater in this group than in the young, in whom such symptoms as persistent cough and sputum, with or without physical signs, cause the sufferer to be referred promptly for a chest X-ray examination.

TABLE I.
Ages at Death (with Tuberculosis), 1955 : Victoria.

Age (Years).	Males.	Females.
0 to 10 ..	1	2
11 to 20 ..	—	2
21 to 30 ..	4	2
31 to 40 ..	3	8
41 to 50 ..	17	7
51 to 60 ..	24	3
61 to 70 ..	38	7
71 to 80 ..	24	3
81 to 90 ..	2	1
91 to 100 ..	1	—
Not stated ..	6	2
Total ..	120	37

Nature and Type of Disease.

Pathogenesis.

From an epidemiological standpoint the aged present some intriguing features. These patients are survivors from an era when active pulmonary tuberculosis was far commoner in the community than it is today. Yet these people are treated in the eve of their lives for an infectious disease which they have presumably encountered on various occasions during their lives. As has already been mentioned, many have evidently had low-grade and sometimes surprisingly extensive tuberculosis for years, which has bothered them but little. The breakdown is part of an aging process, perhaps made more manifest by a stroke or the death of a marital partner.

Others have apparently recent lesions. Whether these are a breakdown of an old primary complex, or a primary infection which has uninterruptedly progressed, is not always clear. Again, odd patients are encountered who have a series of tuberculous foci in various parts of the body, such as bones and joints or the urinary tract. These probably represent breakdowns of foci the result of hæmatogenous spread which took place many years before, and which in old age have become manifest.

In general, sputum contains tubercle bacilli for longer in the aged because the disease tends to be of a fibrotic type, and as a result of the avascularity of the lesions chemotherapeutic agents penetrate less readily. This feature underlines the importance of the aged tuberculous from a public health standpoint.

Mode and Cause of Death.

Cardio-vascular disease is the commonest cause of death among the aged tuberculous. At the post-mortem examination, tuberculous pneumonia superimposed on old fibrocaseous disease may sometimes be revealed as the ultimate

cause. Usually, once the patient obviously starts to lose ground, death ensues rapidly. Senile aged patients with incontinence of urine and fæces and pronounced mental deterioration who linger on for months are not a feature of sanatorium communities.

Some Clinical Features.

Diagnosis.

Chest X-ray examinations, bacteriological examination of sputum and fasting gastric contents and the Mantoux test are used as routine procedures in confirming the diagnosis. Positive Mantoux reactions tend to be weaker in aged subjects than among patients in the prime of life.

Bronchoscopy and bronchography are little used, partly because the patients may be feeble, and partly because information so obtained is largely academic, the patients being unsuitable for surgical treatment for reasons of age.

In the bulk of cases in this group the diagnosis is readily confirmed, but in about a fifth the situation is not clear. "Is it malignant disease with or without tuberculosis?" "Is it a non-specific inflammatory reaction possibly on a bronchiectatic basis?" Such questions may be difficult to answer.

Treatment.

Treatment is on routine lines with rest and chemotherapy. Whenever possible ambulation takes place much earlier than in the younger age group. This is to avoid the well-recognized mental and physical deterioration which sets in when the aged are confined to bed. Streptomycin injections have the disadvantage that they may be painful because of wasting of the subcutaneous tissues. In addition, streptomycin may increase the deafness and giddiness of the aged by causing eighth nerve damage.

PAS, usually given in 0·5 gramme tablets in doses of 12 to 15 grammes per day, may also present some difficulties. The aged exhibit little interest in taking large numbers of tablets daily and more readily than younger patients show manifestations of PAS intolerance.

Attention to the question of well-fitting dentures, to satisfactory optical correction, to hearing defects and to foot defects makes life more pleasant for these patients.

Social Habits.

The aged, on the whole, are very amenable to sanatorium discipline. Although they are often persistent smokers, alcoholism, which may be a troublesome feature in sanatoria, is not a problem among them. The alcoholics presumably die off at an earlier age. Similarly, for obvious reasons, that other potential bugbear of sanatorium life—sex—does not rear its ugly head in the case of the aged tuberculous.

Ultimate Fate.

From the sanatorium standpoint the fate of the patients falls into one of the following categories: (i) the patients die within a few weeks after admission, usually of cardiovascular disease or of tuberculous pneumonia (about one-quarter); (ii) the patients stay on, either because they are too feeble for life elsewhere, or because their home is unsuitable or non-existent or because they are not wanted (about half); (iii) the patients are discharged home under the supervision of their family doctor and of the Tuberculosis Bureau, usually receiving chemotherapy such as PAS and INAH (about one-quarter).

Conclusions.

To the community the main importance of the aged with tuberculosis lies in the possibility of their being an unsuspected source of infection.

As an aid to the earlier detection of this group, routine chest X-ray examinations, when the subject applies for an old-age pension or is superannuated or is being admitted to a home or hospital for the aged, would be of value. Even in a hospital for the aged this group may be a hazard for their young visitors or nurses if their tuberculosis is undetected.

The actual number of persons is not great—they account for about 3% to 4% of admissions to sanatoria. About a third of these patients require institutional care beyond the period necessary for the treatment of the tuberculosis as such, because of the problems of life peculiar to the aged. This period may last for years.

Once the necessity for active treatment of the tuberculosis as such has passed, sanatoria are not ideal institutions for this group, because sanatorium life *et cetera* involves a certain amount of restriction in such matters as coming and going, and the use of tobacco and alcohol.

To deprive an aged person of a few remaining pleasures is not kind; but in running an institution it is hard to treat any given group differently from the rest. A reasonable solution of the difficulty would be a special block attached to a home for the aged and infirm. Aged patients could be transferred to this from the sanatorium after the necessity for more active treatment of the tuberculosis had passed. This would mean that the aged with tuberculosis would be looked after with a minimum of irksome restrictions, and without being a risk to the other inmates of the institution or to the community.

CLINICAL PHOTOGRAPHY AS AN AID TO THE TEACHING OF MEDICINE WITH SPECIAL REFERENCE TO SKIN DISEASES.

By W. KEITH MYERS, M.B., B.S. (Sydney), F.R.C.P. (Edinburgh),

AND

BRIAN FLORANCE, M.B., B.S. (Sydney),

Sydney.

To see or not to see, that is the question.

—ANON.

THE study of medicine, particularly as it affects medical students, in many aspects is essentially a visual one. No amount of descriptive phraseology can convey to the average student the true appearance of many diseases in varied manifestations. This applies especially to skin diseases.

How often in the text-books does one read such a description as the following:

> The eruption characteristically affects the flexor (or extensor) aspects of the limbs, but the whole trunk may be the site of a widespread efflorescence. The lesions, commencing as pin-head size papules of a slightly pink or yellow-pink colour, progress to pea-size nodules or plaques the size of a shilling, reddish or violaceous, which scale, crust or ulcerate, and which may merge or enlarge individually, forming large raised areas of considerable extent.

Just how much does the average student learn from such a description? In the writers' opinion, next to nothing. To see the rash is the thing, and next to that, to see an accurate pictorial representation.

The late Dr. A. C. Roxburgh, when he was in charge of the skin department at Saint Bartholomew's Hospital in London, realized the value of photography, as did his predecessor, the late Dr. H. G. Adamson. A vast collection of photographs depicting the many variants of the common skin diseases was immediately available to each student group during teaching sessions. Prior to the last war these were mainly black and white; but in recent years colour photography has advanced in leaps and bounds, to the extent that it must be considered essential in teaching dermatology. Most teaching hospitals are well equipped with visual aids and a clinical photography department; but the writers were convinced that a modification of the usual "set up" was desirable.

The desiderata for the necessary equipment were considered to be compactness, portability, ease in setting up and rapidity of action. This was best achieved by the

use of a single lens reflex camera, electronic flash equipment, and a portable small projector.

One of us has devised a small fibre suitcase which houses the camera ready for action, the flashgun and powerpack, together with the projector and a flexible lead (Figure I). A small metal case holds the transparency slides for teaching purposes. The small screen is provided by the hospital.

Thus the necessary full equipment can be taken to hospital clinic, to wards or to private consulting rooms. Interesting clinical material can be photographed by flashlight in partly subdued daylight. Prepared slides can be projected instantly by drawing the blinds over the windows of the clinic room. No dark-room or complicated system of fixed lighting is required, and ordinary daylight colour film is used.

With regard to the actual teaching, use is made of the principle of demonstrating the variants of the different diseases under discussion. This was a feature of the skin clinic at Saint Bartholomew's Hospital, whereby each student became familiar with the common skin diseases in all their varied manifestations. Thus the value of a term's short experience is considerably enhanced.

It is manifestly impossible, owing to the limited number of patients presenting at each clinic, for each student to become thoroughly acquainted with all the common skin diseases. The added attraction of visual aids helps to overcome this problem. New and varied clinical photographs are constantly being added to the collection. Thus this method is vastly superior to the use of a standard dermatological atlas. At the end of the session, short lecture-demonstrations can also be given on any particular subject, and, prior to the term clinical examinations, a general quick revision of the subject can be carried out.

The writers have now had some experience of the technical features and difficulties, and endeavour, in the following part of this paper, to set out a standard approach to the subject. The foregoing methods can be applied to many branches of medicine and surgery—for example, the following: (i) plastic surgery; (ii) pathology, especially in the post-mortem room; (iii) general surgery.

Technically the aims are as follows: (i) to produce the best possible photographs in the least possible time and with the simplest efficient equipment; (ii) to have a mobile "set-up" that can be used in rooms and at hospital clinics and in wards; (iii) to keep necessary equipment down to a minimum of weight for ease of transportation.

Equipment.

The equipment consists of a single lens reflex camera with a fast lens, and preferably with a pentaprism type of finder which allows of eye level use. Associated with this is a means of close-up photography, either extension tubes or close-up lenses.

For a light source an electronic flash unit is the best and most mobile.

The equipment used by us is the "Rectaflex" camera with an f.2 "Xenon" lens with presetting lens hood, and a set of close-up tubes which enable us to work as close as two inches to the subject. Associated with this we use an electronic flash of about 65 to 100 joule output.

The carrying case and its contents are shown in Figure I.

The advantages of the single lens reflex camera are as follows: (i) The actual picture to be taken is always seen, which makes for ease of composition. (ii) Focusing is almost automatic. (iii) There is no parallax error in taking the picture. (iv) The camera takes all standard forms of colour film available today. (v) It is easy to work.

The following are the disadvantages of this type of camera: (i) It is usually more costly than other types of camera. (ii) The negative size is so small in black and white that enlargement is always necessary.

The electronic flash has the following advantages: (i) It is extremely mobile. (ii) It does not need power supply for operation. (iii) It is used with the daylight type of colour film, and thus does not need a darkened room. (iv) The exposure can be calculated on the distance from the subject alone. (v) There is no heat to aggravate skin conditions, as there is with "photoflood" type of lighting.

On the other hand, the disadvantages of the electronic flash are the high initial cost, and the fact that the batteries need occasional recharging and/or replacing.

The film used by us at present is "Kodachrome" (k135) daylight type. It has the following advantages: (i) The speed is correct for electronic flash, allowing the use of very small apertures in close-up views where they are most needed. (ii) The film gives beautiful skin tones with the electronic flash. However, a disadvantage is that the film must be sent to Melbourne for processing, and this usually takes about fourteen days.

Close-up effects can be obtained by three methods: (i) the use of extension tubes; (ii) the use of close-up lenses; (iii) the combination of (i) and (ii).

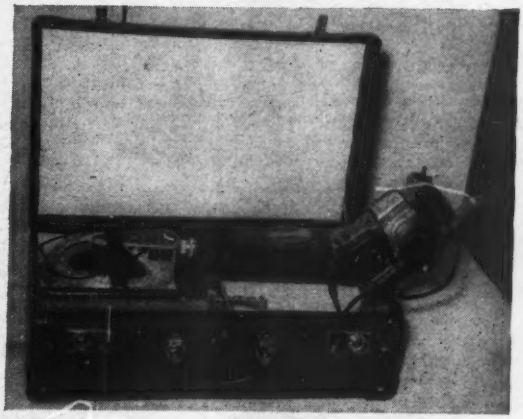

FIGURE I.

Showing the carrying case with the camera swung out and the power pack for flash at the upper right of the case, the projector and flash head at the upper left, and accessories (extension tubes and leads) at the lower left of the case.

Extension tubes are tubes which are placed in behind the lens, increasing its effective focal length. This automatically causes a change in the indicated aperture (f: number) (see Table I). Their advantage is that they have no effect on the optical system of the lens.

Close-up lenses are lenses of 1, 2, 3, 4 and 5 dioptres which are placed in front of the camera lens and alter its focal distance without altering its focal length. These cause no alteration in the indicated aperture, but impair to a slight extent the optical system, as they are not ground to the fine limits of a camera lens, nor in most cases do they have an antireflection coating.

The use of both extension tubes and close-up lenses combines the advantages and disadvantages of the use of either singly.

In recent months a new lens has been added for close-up work. This is the Kilfitt "Macro-Kilar D". This lens has a built-in extension tube, and can be focused down to as close as two inches from the subject. The alteration in exposure is indicated on the side of the lens.

Table I shows the alteration of f: number at major "stop" produced by all the standard extension tubes from 5 to 75 millimetres.

Equipment That is Found to be Most Satisfactory.

A good basic "set-up" would consist of one of the following cameras: "Rectaflex", "Practina", "Exacta Varex" or "Practika" (with a pentaprism fitted), used in conjunction with a "Macro Kilar D" lens or with a normal lens and extension tubes.

TABLE I.
For Use with Lens of 50 Millimetres Focal Length.

Indicated Diaphragm Setting.	Actual Diaphragm Opening.														
2·0	2·2	2·4	2·6	2·8	3·0	3·2	3·4	3·6	3·8	4·0	4·2	4·4	4·6	4·8	5·0
2·8	3·0	3·3	3·6	3·9	4·2	4·5	4·8	5·1	5·4	5·6	5·8	6·1	6·4	6·7	7·0
4·0	4·4	4·8	5·2	5·6	6·0	6·4	6·8	7·2	7·6	8·0	8·4	8·8	9·2	9·6	10·0
5·6	6·2	6·6	7·4	8·0	8·4	9·0	9·6	10·2	10·8	11·2	11·6	12·4	12·8	13·4	14·0
8·0	9·0	9·5	10·5	11·2	12·0	12·8	13·6	14·4	15·2	16·0	16·8	17·6	18·4	19·2	20·0
11·0	12·0	13·0	14·5	15·5	16·5	17·5	19·0	20·0	21·0	22·0	23·0	24·0	25·0	26·0	27·5
16·0	17·5	19·0	21·0	22·5	24·0	25·5	27·0	29·0	30·5	32·0	33·5	35·0	37·0	38·5	40·0
	Extension in Millimetres.														
0	5	10	15	20	25	30	35	40	45	50	55	60	65	70	75

A recent camera on the market is the "Contaflex", which has a fixed lens of 45 millimetres focal length. This camera has the only set of matched and antireflection coated close-up lenses available, and is the only camera of its type. Its advantages are its low cost and its ease of handling.

In association with any of these cameras one of the following flash units could be used: "Blaupunkt Matador" or "Expert II", "Braun Hobby", "Meca Blitz" or "Ce-Be II Perma Flash"—all but the last using wet cell batteries.

The camera and flash unit set up ready for use are shown in Figure II.

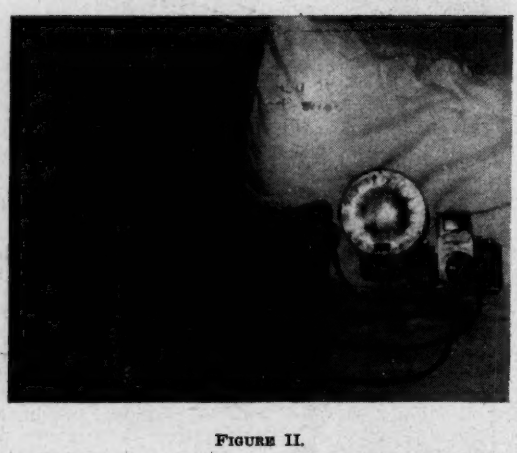

FIGURE II.
Typical "set up"—camera and flash ready for use.

Guide Numbers for Various Flash Units.

The guide numbers for various flash units are as follows:

1. "Blaupunkt Matador": (*a*) "Kodachrome" 30 (half-power), 45 (full power); (*b*) "Agfacolor" 33 (half-power), 48 (full power); (*c*) "Pakolor" 14 (half-power), 20 (full power).
2. "Blaupunkt Expert IIb": (*a*) "Kodachrome", 40 (full power); (*b*) "Anscochrome", 45 (full power).
3. "Ce-Be II": (*a*) "Kodochrome", 45 (full power); (*b*) "Ferraniacolor", 42 (full power).

Films Available for Use at Present.

The following films are available for use at present:

1. "Kodachrome." This gives an excellent colour rendition. Its speed with electronic flash is ideal, but its speed in daylight is a little too slow for normal use. It gives excellent flesh tones.

2. "Agfacolor." This gives results which are similar to those with "Kodachrome", and has an almost identical speed to "Kodachrome" for electronic flash, but is more than twice as fast in daylight. It gives excellent flesh tones.

3. "Anscochrome." This film also gives very good results with electronic flash, but has a very much higher speed, requiring the flash to be reduced in some way—for example, with the use of cutting filters of neutral density over the lens. It is even faster than "Agfacolor" in daylight. It has excellent gradation and exposure latitude. It gives excellent flesh tones.

4. "Ferraniacolor." This gives fair results. It is a little faster than "Kodachrome" to daylight, and slightly slower to electronic flash. Unfortunately it gives brownish or yellowish skin tones.

5. "Fotocolor." This gives fair clinical results, but poor daylight tones. It is about the same speed as "Kodachrome", and needs a compensating filter. It gives violaceous skin tones.

6. "Gevacolor." This film is in very poor supply at present, and has not been used clinically. Results obtained in daylight were very good.

7. "Pakolor." This is the oldest of the negative colour films in this country. It is very slow to electronic flash, but faster than "Kodachrome" to daylight. The prints are poor with flash, but excellent for pictorial scenes.

8. "Agfacolor Negative Film." This has just been released in this country, and to date no results have been obtained.

The Guide Number for Colour Film.

The following is a method of obtaining the guide number for colour film using a cheap black and white film. The black and white film used is "Gevaert Microgram" (27), which gives a guide number four times that of "Kodachrome". The camera and flash are set up at distances of three, six and ten feet from a subject, and a series of exposures on major stops from f4 to f16 are taken at each distance. The film is developed with 30% over-development, and the best result at each distance is taken and the guide number is worked out. The three guide numbers are averaged and divided by four, and this gives the guide number for "Kodachrome".

Conclusion.

The essential thing in photography is to use the equipment and practise with it until all actions become almost automatic.

Summary.

A few ideas on the subject of clinical photography and its uses have been presented, along with a discussion of various types of equipment available and the good and bad features of each type of equipment.

HOW DANGEROUS IS PENTACHLORPHENOL?

By DOUGLAS GORDON,
Director of Industrial Medicine, Department of Health and Home Affairs, Brisbane, Queensland.

NINE times during the last three years official attention has been drawn to patients who have developed an unusual illness (in five cases proving rapidly fatal) after working with pentachlorphenol or its sodium salt. I am reporting our experiences in Queensland with this substance, for it suggests that, as used in industry, it is far more dangerous than we have hitherto been led to believe.

Industrial Uses.

Pentachlorphenol (C_6Cl_5OH) is chemically stable, permanent (low solubility in water and low vapour pressure), relatively cheap and very toxic to fungi, bacteria and other microorganisms. It is natural, then, that it is used to preserve timber, hemp, jute, gums, glues, industrial proteins *et cetera* against moulds. In this State it has been used since about 1948 to protect timber—the latter being immersed in a dipping vat—in a concentration of about 0·5% of active ingredient. This work is carried on under routine stable conditions, and exposure of employees is generally minimal.

Since about 1952 onwards, however, pentachlorphenol (or more particularly its sodium salt, which is soluble in water) has been used increasingly as a weedicide spray, particularly on pineapple farms. Pineapple plants are grown in rows; they have a shallow rootage system which is damaged by inter-row mechanical tillage. Therefore, cultivation has to be carried on by hand chipping with a labour force which has become more and more scarce and costly. An efficient economical weedicide which does not damage the plants or contaminate the product is therefore of great importance to an industry which has to keep a wary eye on competitors from cheap labour countries. To make up the spray 10 pounds of sodium pentachlorphenate powder are added to 100 gallons of water, usually with three gallons of mineral oil as well. This gives a concentration of 1% active ingredient. However, farmers, being great individualists, vary this formula greatly, most frequently increasing rather than decreasing the strength. The spray is delivered to the ground either from a knapsack spray carried on the back (this holds three to four gallons), or from a power spray outfit used on a truck or trailer. The latter is parked on the headland of the pineapple patch and a long hose line with a spray "gun" at its end is carried backwards and forwards between the rows of plants. Apart from inhalation of the spray, spillage from over-full containers and leaking joints and connexions frequently causes skin contamination, as does also the actual spray mist.

Review of Previous Experience.

1. Since the first days of its use this substance has been recognized as a particularly bad irritant of body surfaces. (Carelessly handling the powder for the first time is really an unpleasant experience.)

2. Opinions in regard to systemic poisoning, however, of late years have always tended towards optimism.[1] (*a*) This optimism was probably not altogether well founded, for from 1938 to 1943 animal experiments, mainly in the United States, showed that it was a toxic substance, and that it was readily absorbed through the skin (Fairhall, 1949). (*b*) Industrial hygienists, however, tend to be concerned not so much with toxicity *per se* as with poisonings occurring in actual industrial use. (D.D.T., for instance, is an example of a poisonous substance which in use causes very little trouble.) Barnes in his World Health Organization Monograph, which has become a "vade-mecum" for those working in this field, well summarized the position in 1953 as follows:

> Serious intoxication in man from pentachlorphenol has not been recorded, but it must be handled carefully in order to avoid contact with the skin, as it readily produces dermatitis. Recently, a group of cases of transient sciatic neuralgia has been described among men who were shovelling the compound in a manufacturer's plant.

In 1955 Edson lists pentachlorphenol as comparatively safe. However, a footnote states that it has not yet been evaluated. (*c*) My own relatively happy outlook had been disturbed during 1953 by the first two Queensland patients, and my grave doubts were then confirmed by sighting an abstract at the end of 1953 reporting two deaths from the timber industry in France (Truhaut *et alii*, 1952). A further abstract seen here at the end of 1954 recorded a fatal case in Japan (Nomura, 1953). The death of a man handling pentachlorphenol has now also occurred in New South Wales (Jones, 1955).

In view of the rapidity with which we seem to have encountered trouble here once the "P.C.P.", as it is popularly called, came into common usage as a weedicide, the paucity of warnings in trade, chemical and medical literature is remarkable.

Clinical Experience.

Queensland experience to date is summarized in Tables I, II and III. The first seven cases were reported at a time when "P.C.P." was still popularly believed to be relatively harmless. Doctors working in widely scattered areas reported the cases because they were puzzled by a clinical sequence of events which was unusual and which they could not explain by any known disease entity. In each case in which death occurred, the attending doctor had refused a death certificate. In the circumstances I doubt whether we are reading into some known disease entity the diagnosis of a poisoning. Case VIII—a mild case—was reported because by then the medical profession had been warned about pentachlorphenol, and Case IX—the last—because by now the pineapple industry is aware of what has been happening.

The failure to find pentachlorphenol by analysis of organs obtained from autopsy had until the last case been the most puzzling hurdle, and this factor has prevented an earlier report. These negative chemical findings made me think that the patient in Case I was probably an elderly man who had died from a fulminating attack of scrub typhus, the more particularly since at the time I was not informed how quickly death took place after onset of symptoms. Fortunately, a senior colleague who saw the records was more suspicious (Hirschfeld, 1954). Later, another colleague suggested that larger quantities of autopsy material should be taken for analysis (Holden, 1955). When the death occurred recently of the patient in Case IX, the analyst was supplied with large quantities of material, his method of analysis was changed somewhat and his results then recorded quantities of pentachlorphenol in all tissues. Since Case IX ran a course clinically very similar to all the other cases except Case III, and taking into consideration the common experience of exposure to "P.C.P.", I feel justified in suggesting that we have been dealing with patients suffering from pentachlorphenol poisoning.

If these severe cases are due to "P.C.P.", the question naturally arises whether less serious and frequent attacks of poisoning due to this substance are occurring among its users. If they are, I doubt whether the ill-health is serious enough to seek medical attention for such attacks, for I have questioned medical practitioners in the main pineapple areas on this point. However, there is some good evidence from the farmers themselves that they do frequently experience transient mild ill-health from using "P.C.P.". A number of farmers have told me that after spraying "P.C.P." they have had a few days' nausea, anorexia and mild abdominal pain, not necessitating medical attention.

[1] One piece of applied research that was freely quoted from American sources when the substance was first introduced in Queensland concerned an investigator who took a bath in a dilute solution to show how harmless the substance was. When police were looking into the death of the first patient recorded here, they were informed, as proof of how groundless their suspicions were, that a fellow worker had in mistake drunk a cupful of the spraying solution without ill effects.

TABLE I.

Case Number.	Patient's Age. (Years.)	Date of Onset.	Place.	Attending Doctor.	Occupational Details.	Outcome.
I	58	26. 2.53	Tully, North Queensland.	Dr. A. B. Maruff.	During the three to four weeks before onset was spraying weeds on sugar-cane tram-line. Knapsack spray. Did not mix spray. Sodium pentachlorphenate, 1·5% concentration.	Died about 16 hours after onset.
II	47	9.12.53	Nambour, Queensland.	Dr. J. E. Trotter and associates. Dr. J. C. Moffatt.	Spraying weeds in pineapples the day before onset of illness. Used sodium pentachlorphenate. Other details unknown. Did not go to hospital until seven days after onset.	Gradually recovered about 14 days after onset.
III	40	5. 3.54	Cairns.	Dr. D. C. C. Sword and Brisbane General Hospital staff.	Had worked for many months at a sawmill, operating kilns in which timber which had been soaked in sodium pentachlorphenate solution (0·15% maximum concentration) and boron (0·2%) was being dried. Hazard on inspection was not obvious. Gradual onset of symptoms. Timber was not handled by hand.	Recovered completely after about four months in hospital.
IV	40	8.12.54	Brisbane.	Dr. R. P. Schmidt and Brisbane General Hospital staff.	Spent 15 hours in all during the three days preceding onset spraying weeds around a factory. No previous exposure. Used knapsack. By mistake 14% pentachlorphenol in dieseline used. Did not mix spray himself. Overalls soaked in fluid.	Died about 30 hours after onset.
V	14	6. 1.55	Gympie.	—	Sprayed pineapples for a full day mixing the spray himself. Used knapsack. Solution subsequently analysed and found to contain 2·5% active ingredient sodium pentachlorphenate. In previous weeks had done a few days' or a few hours' spraying off and on.	Died within 18 hours without medical attention.
VI	35	14. 3.55	Bundaberg.	Dr. L. S. Stark and Brisbane General Hospital staff.	For three days before onset had sprayed weeds on sugar-cane tram-lines. Used horse-drawn railway truck with power spray unit. Had done this work on several occasions before during the summer. Used pentachlorphenol oil emulsion; six gallons of emulsion to 240 gallons of mineral oil, with 12 pounds of trichloracetic acid. Wore long trousers and shirt, but contamination of skin frequently occurred.	Recovered without sequelæ in about five weeks.
VII	16	30. 3.55	Nambour.	Dr. J. C. Moffatt.	Was mixing pentachlorphenate solution, about 1·0% concentration. Siphoned some of the water into another container. Thinks he swallowed a little of the solution. Did not do any spraying. This happened at 8.45 a.m. Symptoms came on at 3 p.m.	Died about nine hours after onset of symptoms.
VIII	—	4. 5.55	Brisbane.	Dr. D'Arcy Kelly.	Pineapple worker. Had on two occasions consulted his doctor with abdominal pain which had on each occasion come on after a day's spraying. All investigations gave negative results except for an apparently increased quantity of "P.C.P." in the urine.	Very mild illness. Patient recovered.
IX	16	10. 1.56	Glasshouse Mountains.	Dr. D. Millar, Caboolture, and Staff, Brisbane General Hospital.	For previous four weeks sprayed weeds in pineapples one or two days a week for two or three hours on each day. Power spray unit. ?1·0% solution of sodium pentachlorphenate. Did spraying on January 9, 1956. Taken ill at midday on January 10. Wore shorts—usually a shirt. No footwear. Scratches and cuts on legs and feet.	Died about 21 hours after onset.

Discussion.

Clinical Syndrome.

The data presented in this paper suggest a clinical picture common to all except one of these patients. The onset is usually marked by some abdominal symptom (pain, nausea, vomiting). Later profuse sweating is noticed by all observers, and sometimes the patient complains of intense thirst. If the patient is going to die, he will probably do so in the first twenty-four hours, and in the last hour or two he rapidly changes from a patient who is not remarkably sick to one who is completely moribund. The temperature is only moderately elevated, the pulse rate is extremely rapid and the respirations are also increased. The sweating, incidentally, is a very real thing. In one patient who recovered, the bedclothes were continually soaked with sweat in spite of repeated changes of linen. This sweating has been recorded spontaneously in the clinical notes by all attending doctors.

Routine laboratory investigations do not seem to help the diagnosis, though admittedly remoteness of the areas and rapidity of death prevented very full use of ancillary aids.

Case III differs clinically from all the others, and this patient's field exposure is also different from them. His exposure was in a different industry, and was more constant and continual, but presumably to lesser concentrations of the material, and the exposure had occurred over a long time day after day. Perhaps, therefore, this patient's syndrome of hepatic enlargement with possible reversible toxic myocarditis represents a chronic condition.

The acute syndrome reminds one somewhat of poisoning by dinitro-ortho-cresol, and eventually I think that pentachlorphenol will be shown to act similarly to that substance in the human body.

Field Observations.

A number of interesting suggestions have cropped up in relation to the reason why Queensland has had this unusual experience with pentachlorphenol; huge amounts of it, for instance, are used in Hawaii without any ill-effects (Carter, 1955). It has been suggested that, like dinitro-ortho-cresol, hot weather enhances its toxicity. This may be so, but my series cannot be used to prove it, for the maximum use of pentachlorphenol takes place during the hot summer months in Queensland, which are also the months of maximum weed growth. In consequence, the fact that our patients became ill in the summer or at its end is not necessarily of any significance.

For the benefit of those industrial hygienists who look on the handling of concentrated solutions with suspicion, it is interesting to note that in at least two of the fatal cases the patient had nothing whatsoever to do with the mixing of the spray.

Some of our troubles may be due to the peculiar individuality of independent white workers in the tropics, who desire to order their dress and habits as they wish. In two of the fatal cases the spray used was of a greater concentration than that recommended, and in a third the patient had siphoned the pentachlorphenate solution from one container to another and in the course of doing so "thought" he had swallowed some of it. Perhaps continual skin contamination accounts for a lot of the trouble. Shorts, often without a shirt, are worn everywhere in farming operations, and some of the patients wore no footwear. In pineapple farming unprotected lower limbs are scratched by the serrated pineapple leaves, and in this particular type of spraying the spray is directed down on to the ground and not up into the air on to foliage. This reduces inhalation of the spray, but increases the contamination of

TABLE II.

Symptoms and Signs.

Case Number.	Symptoms.				Signs.
	Abdominal Symptoms at Onset.	Thirst.	Sweating, Fever.	Other.	
I	Present.	Present.	Present.	Aches and pains in limbs and chest.	Temperature, 103° F. Pulse rate, ? 160 per minute. Respirations, ? 56 per minute. Rash on trunk. Died.
II	Present.	Present.	Present.	Excessive fatigue.	Temperature, 101·5° F. Pulse rate, 104 per minute. Respirations, 40 per minute. Fine rash ? miliaria. Recovered in a few weeks.
III	Present.	Present.	Present.	Aching calves, tiredness, weakness. Dyspnœa on exertion.	Temperature, 101° F. Pitting œdema of lower limbs. Tender liver edge. Later gynæcomastia and enlarged left ventricle in the X-ray film. Investigations gave results within normal limits. Completely recovered in about four months. However, in this patient all these signs and symptoms were of gradual onset and had been present two or three weeks when he was first examined by a doctor. In the other patients the onset of symptoms was rapid.
IV	Present.	Absent.	Present.	Non-productive cough.	Temperature, 104·5° F. Pulse rate, 156 per minute. Respirations, 28 per minute. Cloud of albumin in urine. Disorientated. Died.
V	Present.	Present.	Present.	——	Was not examined by a doctor before death.
VI	Present.	Absent.	Present.	——	Some rise in temperature. ? Urinary infection and palpable spleen. Recovered in about five weeks.
VII	Present.	Absent.	Present.	——	Normal temperature. General muscular spasm before death. Difficulty in breathing. Died.
VIII	Present.	Absent.	Absent.	——	No abnormality found on examination. Mild case. Seven milligrammes of pentachlorphenate per litre of urine found immediately after spraying.
IX	Present.	Present.	Present.	——	Temperature, 100·8° F. Pulse rate, 160 per minute. Respirations, 28 per minute. General flaccidity. Acetone breath. ? Slight neck stiffness. Pronounced rigidity immediately after death.

TABLE III.

Autopsy Reports: Principal Abnormal Findings Only.[1]

Case Number, Date.	Patient's Age. (Years.)	Attending Doctor.	Findings.
I: February, 1953.	58	Dr. E. J. Ryan, Tully, North Queensland.	Macroscopic appearances: scarred aortic valve, cirrhotic liver, nothing else. No microscopic examination made. Small portions of kidney, liver, spleen, heart and lungs sent to Brisbane (nearly 1000 miles away) for analysis. No pentachlorphenol found.
IV: December, 1954.	40	Dr. M. J. O'Reilly, Brisbane.	Macroscopic appearances: Blood-stained pus in trachea and bronchi. Lungs: large, heavy and congested. No definite consolidation. Gross œdema. Small areas of bronchopneumonia near hilum of each lung. Liver: large and pale; nutmeg effect on cut surface. Kidneys: large, pale, œdematous. Microscopic appearances: Lung: gross congestion of all vessels with many areas of recent intraalveolar hæmorrhage. A few macrophages in one or two areas, but generally no reaction to hæmorrhage could be seen. No inflammatory reaction except some lymphocytic infiltration in subpleural tissues. Liver: pronounced centrilobular congestion and accumulation of bile pigment in centrilobular cells, and an occasional one showing early necrosis. Widespread fatty degeneration of liver cells. Very slight lymphocytic infiltration of some portal tracts. Kidney: congestion of medulla and peripheral cortex. Liver and blood submitted to analyst—no pentachlorphenol found.
V: January, 1955.	14	Dr. L. M. Outridge, Gympie.	Macroscopic appearance: Small hæmorrhages at base of heart. Lungs: numerous hæmorrhagic areas, especially at bases; some yellowish (pale) and, in some areas, frothy fluid exuded from cut lung surface. Spleen: enlarged. Liver: cut section of liver had a mottled appearance. Microscopic appearance (Dr. J. I. Tonge, Brisbane): Liver: moderate congestion of central zone of liver lobules. Heart: a few small scattered hæmorrhages in subpericardial fatty tissues. Lung: generalized congestion and pulmonary œdema. The alveolar walls were engorged and hæmorrhage had occurred into many alveoli. The air sacs were distended with œdema fluid. There was slight peribronchial round-cell infiltration, and the terminal bronchioles contained red cells, pus and some desquamated epithelium. Portions of stomach, spleen, kidney and liver were submitted to the analyst, but no pentachlorphenol was found.
VII: March 31, 1955.	16	Dr. F. J. Short, Nambour.	Macroscopic appearance: little of significance noted. About a dozen enlarged mesenteric glands and uniformly reddened pulmonary and tricuspid valves. No microscopic examination was made. The analyst found a trace of pentachlorphenate in the liver, but none in the stomach, kidney or spleen. (This patient had probably swallowed some spraying solution.)
IX: January 12, 1956.	16	Dr. J. I. Tonge, Brisbane.	Macroscopic appearance: Trachea: slight congestion and œdema in lower third of trachea extending into both main bronchi. Lungs: slight congestion and œdema in both lower lobes, but otherwise nothing significant. Liver: on the cut surface there were seen to be some ill-defined pale brownish yellow areas which were scattered throughout the liver tissue, and these were irregular in shape and stood out in contrast to the darker normal liver tissue. The cut surface had a somewhat cloudy and glossy appearance. Microscopic appearance: Heart: some peculiar degeneration of intravascular leucocytes and some fragmentation of occasional muscle fibres. Lung: some passive congestion, patchy collapse and slight alveolar hæmorrhage. Analyst's report: Pentachlorphenol content, milligrammes per 100 millilitres or per 100 grammes: blood, 5; urine, 7; lung, 14·5; kidney, 9·5; liver, 6·5; brain, 2·0.

[1] In view of the fact that the reports are made by two different pathologists, there is similarity between the autopsy reports in Cases IV and V.

bare legs and feet. I am led to believe that in other hot countries where "P.C.P." is used, native labour is rigidly controlled in the manner in which it is used, and in the type of protective clothing which must be worn.

The fact that some of the patients have been adolescents probably does not mean much, unless we know the proportion of the total amount of spraying which is done by people in this age group.

The amount of time required to produce what would seem to be poisoning is very difficult to estimate, because the actual time spent spraying is hard to elicit. The patient in Case I had sprayed for several weeks, and died at the end of that period. The patient in Case IV had sprayed for fifteen hours only, but he had used a grossly concentrated solution. In Case V the patient, a lad, aged fourteen years, had sprayed a 2·5% solution for a full day only, immediately before becoming ill, but he had done in previous weeks odd hours and odd days of spraying, and his experience was fairly typical of most people's in the pineapple industry. That is to say, they might do one or two days' spraying each week during the summer and perhaps on these days spend only a few hours on actual spraying.

Autopsy Reports.

In Cases I, VII and IX, little of significance was found at autopsy, though admittedly no histological examinations were made in Cases I and VII.

In Cases IV and V the microscopic appearances in the lungs were similar; they can be summarized by the statement that in both cases the lungs had the histological appearance of gross congestion and widespread intra-alveolar hæmorrhage, with very little sign of inflammatory reaction.

In looking at this, it must be remembered that two of the patients (Cases VII and IX) with relatively negative autopsy reports had produced other evidence of pentachlorphenol absorption. The patient in Case VII considered that he had swallowed some spraying solution, and in the tissues of the patient in Case IX pentachlorphenol was found in quantity.

It is obviously impossible to discuss these apparent discrepancies with any certitude. It may perhaps be a nice theory to suggest that the lesion varies according to the mode of absorption—that is, that pulmonary congestion and intraalveolar hæmorrhages result when pentachlorphenol is breathed into the lung—but there is no proof that this is so.

Treatment.

Treatment up to the moment seems to be entirely symptomatic. Edson (1955) has suggested the use of chlorpromazine as a therapeutic measure, particularly *in extremis*, acting on the theory that pentachlorphenol may be speeding up the metabolism and chlorpromazine may tend to lower it. He has also pointed out that there is some experimental evidence that hydrocortisone benefited rats poisoned with dinitro-ortho-cresol. By and large the position at the moment is not very helpful.

Prevention.

In theory prevention is simple. Those who use the substance should wear a suitable mask and full protective clothing. In practice this is very difficult to attain with farmers in a warm to hot climate. However, by the use of relatively simple measures of protection, and by publicity concerning the troubles that have arisen in the use of pentachlorphenol, I am reasonably optimistic that the present position will be greatly improved.

Summary.

1. During the last three years in Queensland nine male subjects have developed unusual illnesses after working with pentachlorphenol or its sodium salt. Five of these died very quickly.

2. Eight of these patients had rather similar symptoms and signs. The ninth had a more chronic exposure to "P.C.P." and had a somewhat different type of illness.

3. Some notes concerning field exposure, clinical details and autopsy findings of these patients are given.

4. It is suggested that the illness described is due to pentachlorphenol.

Acknowledgements.

This is obviously a compilation of the records of patients in the care of many and various medical practitioners whose names are reported in Table I. I thank them all sincerely for supplying me with full details of their patients, and I congratulate them on their clinical acumen in recognizing at once the significance of an unusual case. I thank the several Government medical officers and pathologists who performed the autopsies (*vide* Table III). I thank Mr. I. Henderson, of the Government Chemical Laboratory, for his interest in the analytical problem, and for his performance of the various chemical analyses. I wish to thank Mr. W. Flewell-Smith, of the Committee of Direction of Fruit Marketing, representing the pineapple industry, local representatives of the manufacturing companies, and officers of the Forestry Department and of the Department of Agriculture and Stock, for their cooperation, advice and help. I thank the Director-General of Health and Medical Services, Queensland, for permission to publish this article.

References.

BARNES, J. M. (1953), "Toxic Hazards of Certain Pesticides to Man", World Health Organization, Geneva.

CARTER, W. (1955), Head, Entomology Department, Pineapple Research Institute of Hawaii, Honolulu: personal communication to Dr. S. H. Trout, Department of Agriculture and Stock, Brisbane.

EDSON, E. F. (1955), "Emergencies in General Practice: Agricultural Pesticides", *Brit. M. J.*, 1: 841.

EDSON, E. F. (1956), personal communication.

FAIRHALL, L. T. (1949), "Industrial Toxicology", Williams & Wilkins, Baltimore, 415.

HIRSCHFELD, O. E. (1954), personal communication.

HOLDEN, H. F. (1955), Walter and Eliza Hall Institute, Melbourne: personal communication.

JONES, A. T. (1955), Scientific Officer, Division of Industrial Hygiene, Sydney: personal communication.

NOMURA, S. (1954), "Studies on Chlorophenol Poisoning. Rep. 1. A Clinical Examination of Workers Exposed to Pentachlorophenol" (abstract), *Bull. Hyg.*, 29: 294.

TRUHAUT, R., L'ÉPÉE, P., and BOUSSEMART, E. (1953), "Occupational Poisoning in the Wood Industry. Observations on Two Fatal Cases" (abstract), *Bull. Hyg.*, 28: 556.

Reports of Cases.

HEREDITARY RED CELL APLASIA.

By I. S. WALLMAN, M.B., M.R.A.C.P., D.C.H.,
Senior Medical Registrar, Princess Margaret Hospital for Children, Perth, Western Australia.

PURE red cell aplasia is a rare but increasingly recognized entity. It is most commonly seen in the congenital hypoplastic anæmia of Diamond and Blackfan. In this condition from early infancy there is hypoplasia amounting at times to complete aplasia of the red cell marrow. There is no involvement of the platelets or myeloid series, and the only treatment of value is repeated blood transfusions. A small proportion of children with this condition eventually have spontaneous remissions (Harper and Geikie, 1955).

Red cell aplasia may also result from the toxic action of certain drugs, and Strauss (1943) reported a case following sulphathiazole administration in which a spontaneous cure occurred three weeks after administration of the drug was stopped.

Recently a similar blood disorder has been recognized in association with thymic tumours (Chalmers, Marshall and Boheimer, 1954; Ross, Finch, Street and Streider, 1954). Although the exact relationship between the two is not known, it is interesting that thymectomy produced a temporary hæmatological remission in one of two cases

described by Chalmers *et alii*. Cortisone also produced remissions in these cases.

Loeb, Moore and Duback in 1953 elaborated the concept of chronic bone marrow failure and included hypoplastic anæmia in this group under the heading of primary erythroid hypoplasia. They described the cases of two brothers with this condition, in both of which severe anæmia was first noted at the age of seventeen years. In the elder brother, after five years of blood transfusions a short remission was obtained with ACTH, and then two months later another remission was obtained with splenectomy. After a temporary relapse, a seven months' course of cortisone appeared to induce a complete cure, and in the last two years of the study no blood transfusions were required. The younger brother was given transfusions regularly for two years, and appeared to have a permanent remission after splenectomy.

Various other reports of red cell aplasia have appeared, and the response to cortisone and ACTH has been variable (Erslev, Iverson and Lawrason, 1952-1953). Fountain and Dales (1955) reported apparent improvement with cobalt chloride in a woman in whose treatment splenectomy had been of doubtful value.

The present report deals with two cases of pure red cell aplasia occurring in father and daughter, in one of whom a favourable response was obtained with cortisone.

Case I.

In December, 1944, when he was aged thirty-four years, A. first developed symptoms of dizziness, breathlessness and weakness while he was in the army. Apart from severe pallor, no abnormal clinical signs were found on examination. The blood picture showed a normochromic normocytic anæmia, the red cell count being 1,320,000 per cubic millimetre, the hæmoglobin value 4·0 grammes *per centum* and the white cell count 3050 per cubic millimetre. During the next twelve months he received 12 blood transfusions, together with iron and liver preparations.

From January, 1946, to February, 1949, he had a partial remission, and although he had mild symptoms, he required no blood transfusions and was able to work as a plasterer. He was given numerous hæmatinics during that period, including iron, liver and folic acid, but without apparent effect. The hæmoglobin value varied between eight and 11 grammes *per centum*, and the red cell count between 2,500,000 and 3,500,000 per cubic millimetre.

In August, 1949, he had an exacerbation, and the hæmoglobin value fell to 3·2 grammes *per centum* and the red cell count to 850,000 per cubic millimetre. The white cells numbered 6000 per cubic millimetre, the differential count being normal, and the proportion of reticulocytes was 0·2%. The red cells were hyperchromic and macrocytic. Bone marrow examination revealed severe hypoplasia of the red cell series, but no abnormality of the white cells. The gastric juice was normal.

Since August, 1949, the patient has required regular transfusions of packed cells approximately every six weeks, the hæmoglobin value falling to six to seven grammes *per centum* at the end of this period. The need for transfusion has been gauged by the patient's symptoms. With this treatment he continued to work until March, 1955. Repeated blood counts have revealed severe anæmia of hyperchromic, macrocytic type, and absent or greatly reduced reticulocytes (0 to 0·5%). The white cell count and platelets have been normal throughout.

In 1952, further investigations were carried out, with the following results. The bleeding time was five and a half minutes, the clotting time was four minutes and the prothrombin concentration was 45%. The test for occult blood in the fæces and Coombs's test both gave negative results. Further examination of the bone marrow revealed almost complete aplasia of the red cell series, with a myeloid-erythroid ratio of 11:1.

The patient's skin became increasingly pigmented, and in January, 1954, he presented the typical picture of hæmosiderosis, with greyish-brown skin, large liver and testicular atrophy. Liver function tests revealed a thymol turbidity of 14 units, but no other abnormality. He was also found to have mild diabetes, which was stabilized on a daily dosage of 24 units of protamine zinc insulin and 20 units of soluble insulin.

In July, 1954, he was given a nine-day course of cortisone (a total of one gramme), but there was no response to this, and the reticulocyte level remained below 1%.

Another course of cortisone, 25 milligrammes per day, was commenced in July, 1955, but again there was no response. Attempts to increase the dose beyond this figure have been unsuccessful because of difficulty in controlling the diabetes.

At present his skin is grossly pigmented, and he has considerable liver enlargement and some mild ankle œdema. His diabetes is stabilized with a daily dosage of 58 units of protamine zinc insulin and 30 units of soluble insulin, and he is having each day 25 milligrammes of cortisone and 0·25 milligramme of "Digoxin". Transfusions are being given every three to four weeks.

Case II.

L., a girl, aged six years, daughter of A., presented in July, 1955, with a history of increasing pallor for three months. The mother is well and has a normal blood picture, but the father has been treated for "hypoplastic anæmia" for twelve years. There are no other children, and no other family history of anæmia. No bleeding tendency had been noted, and there was no history of exposure to chemicals or of ingestion of drugs.

The only positive findings on examination of the child were severe pallor, a widespread systolic murmur in the precordium, and slight pitting œdema of the ankles. The blood pressure was 120 millimetres of mercury, systolic, and 75 millimetres, diastolic.

A number of investigations were carried out. The hæmoglobin value was four grammes *per centum*. The red cell count was 1,700,000 per cubic millimetre; the white cell count was 9500 per cubic millimetre, 39% being neutrophile cells, 14% eosinophile cells, 1% basophile cells, 41% lymphocytes and 5% monocytes. The red cells were normocytic and normochromic. No reticulocytes were seen. Platelets were plentiful. The red cell fragility and the bleeding and clotting times were all normal. Coombs's test produced a negative result. The urine was normal. Examination of the bone marrow revealed pronounced hypoplasia of erythrogenic tissue, but no evidence of arrest of maturation. The myeloid series was normal apart from a moderate increase in the number of eosinophile cells.

A transfusion of packed cells was given on July 13, and was followed by a rise in hæmoglobin value to 10·5 grammes *per centum*; but over the succeeding five weeks there was a progressive fall to seven grammes *per centum*. A five weeks' course of cobalt sulphate therapy was commenced on August 10, but a further transfusion was necessary a week later and the rate of fall of the hæmoglobin level was unaffected (see Figure I). On September 23, when the hæmoglobin value was seven grammes *per centum*, the administration of cortisone, 75 milligrammes per day, was begun, and after one week the reticulocytes had risen to a level of 16%. After this there was a progressive rise in the hæmoglobin value to 12 grammes *per centum* over a period of five weeks. A bone marrow examination four weeks after the commencement of cortisone therapy revealed hyperplasia of the red cell series (myeloid-erythroid ratio, 1·5:1), and there was an increased percentage of pronormoblasts and basophilic normoblasts. The high initial eosinophile cell count gradually subsided, and apart from a transient rise in the leucocyte count the white cell series has been normal. Platelets have been plentiful throughout. The dose of cortisone was gradually reduced, and its administration was finally discontinued on February 10, 1956. The hæmoglobin value has varied from 10 to 13 grammes *per centum* over the past four months without further transfusions.

On February 20, 1956, the patient was a healthy, active child, and was apparently normal.

Discussion.

The similarity of the blood disorders is so striking in the two cases presented that it seems rational to assume a common ætiology. In the absence of any toxic factor, an hereditary defect of the bone marrow appears the most likely explanation.

The blood picture in both cases is one of severe anæmia with reticulocytopenia and hypoplastic red cell marrow. The father's disease appears to have started at the age of thirty-four years, and although he had a partial remission lasting for three years, the blood picture in the past seven years has been one of almost complete aplasia. In the later years the anæmia became hyperchromic and macrocytic in type. The prognosis, in the presence of severe hæmosiderosis and diabetes, is poor.

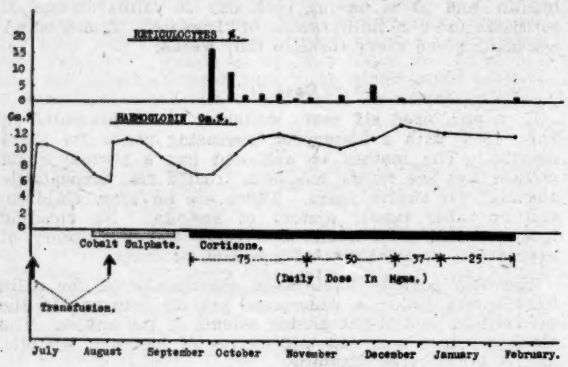

FIGURE I.

The child's anæmia began at the age of six years, and the only difference in her blood picture from that of her father is the initial transient eosinophilia. Examination of the bone marrow revealed a similar hypoplasia of red cell precursors, with complete absence of reticulocytes in the peripheral blood.

Although one cannot completely exclude a thymoma without surgical exploration, the presence of normal chest X-ray findings and the association of a similar condition in two members of one family make this unlikely.

There seems little doubt that the cortisone was responsible for the remission in the girl. The failure of the father's condition to respond may have been due to the late stage at which cortisone therapy was started, and to inadequate dosage.

The only other reference to hereditary pure red cell aplasia in the literature is that of Loeb *et alii*, and it is interesting that cortisone also produced a remission in the one case in which it was tried.

These observations give further support to the view that certain types of bone marrow failure may be relieved by cortisone or ACTH, and suggest that there may be a special group of red cell aplasias which are both familial and reversible.

From Loeb's work it would appear that if a remission is obtained with cortisone or ACTH, then one can also expect improvement with splenectomy. For this reason this operation will probably be carried out if the girl develops a recurrence of her anæmia.

Summary.

The various forms of red cell aplasia are discussed. It occurs most commonly in the congenital hypoplastic anæmia of Diamond and Blackfan. Less commonly it follows the ingestion of certain drugs; it has recently been reported in association with thymoma, and it may also occur as an hereditary defect of the bone marrow. The effects of cortisone and splenectomy are considered.

Two cases of pure red cell aplasia occurring in father and daughter are described. Cortisone produced a prolonged remission in the child, but no response in the father, in whom the lack of response may have been due to the late stage at which the cortisone was given and to inadequate dosage.

Acknowledgements.

I should like to thank Dr. C. W. Lankester for allowing me to publish details of the child, and Dr. G. A. James for performing the hæmatological investigations.

References.

CHALMERS, J. N. M., and BOHEIMER, K. (1954), "Pure Red Cell Anæmia in Patients with Thymic Tumours", *Brit. M. J.*, 2:1514.

ERSLEV, A. J., IVERSON, C. K., and LAWRASON, F. D. (1952-1953), "Cortisone (Adrenocortical Preparation) and A.C.T.H. (Adrenocorticotrophic Hormone) in Hypoplastic Anæmia", *Yale J. Biol. & Med.*, 25:44.

FOUNTAIN, J. R., and DALES, M. (1955), "Pure Red Cell Aplasia Successfully Treated with Cobalt", *Lancet*, 1:541.

HARPER, M., and GEIKIE, G. (1955), "Congenital Pure Red Cell Anæmia or Erythrogenesis Imperfecta", M. J. AUSTRALIA, 2:245.

LOEB, V., junior, MOORE, C. V., and DUBACK, R. (1953), "Chronic Bone Marrow Failure", *Am. J. Med.*, 15:439.

ROSS, J. F., FINCH, S. C., STREET, R. B., junior, and STREIDER, J. W. (1954), "The Simultaneous Occurrence of Benign Thymoma and Refractory Anæmia", *Blood*, 9:935.

STRAUSS, A. M. (1943), "Erythrocytoplasia Following Sulphathiazole", *Am. J. Clin Path.*, 13:249.

Addendum.

Since this article was written the girl's hæmoglobin value has fluctuated, but has never fallen below nine grammes *per centum*. Her health has remained good throughout, and no further cortisone has been given. Splenectomy has not been performed.

Reviews.

The Cow Jumped Over the Moon: Private Papers of a Psychiatrist. By R. S. Ellery; 1956. Melbourne: F. W. Cheshire. 8¾" × 5½", pp. 287. Price: 18s. 9d.

A LITERARY CRITIC remarked that when a doctor writes well he writes very well, and many readers of the posthumously published autobiography of Dr. Reginald Ellery will regard this book as a notable contribution to Australian literature. From early adolescence Reg Ellery, as he was known to his friends and colleagues and in various literary circles, was a book lover and a book collector; he read voraciously, had a retentive memory, possessed a discriminating sense of the value of words and wrote fluently. That a young man of his artistic temperament should choose insanity as the central pivot of his career may seem curious, but he brought to his work a greater stability of constitution and disposition than might have been expected. His connexion with the Victorian Lunacy Department was not a happy one, for he found the premises overcrowded and insanitary and the attendants more interested in their salaries and their "perks" than in the welfare of their patients. The medical staff was utterly inadequate for the heavy demands made on them. Ellery's vigorous introduction of administrative reforms aroused opposition, and a conspiracy to thwart him developed amongst the non-medical staff which was supported by a weekly newspaper and certain not very admirable politicians. This miserable story is told with but little evidence of temper; indeed the only marked departure from a balanced calm is to be found in his account of his subsequent dealings with the Medico-Legal Society, which he believed to be an attempted union between two utterly incompatible moieties. Ellery travelled extensively to increase his knowledge of psychiatric treatment, and in 1931 severed his connexion with the Lunacy Department and embarked on private practice which soon became extensive and fairly lucrative. This autobiography will be studied by medical and other historians for information regarding the introduction of new methods of treatment; most of Ellery's claims to priority will probably be conceded by the few expert psychiatrists still with us who were his contemporaries; possibly one of these claims will be challenged, namely, that he introduced insulin treatment, for there is evidence that Dr. Clive Farran-Ridge may have preceded Ellery; at least he should share the honour of the Australian inception of this remedial measure.

The book has, however, far greater claims on our regard than its exposition of psychiatric theory and practice, for

here will be found the opinions and judgements of an alert and highly trained intellect with many sane and penetrating analyses of social conditions and human behaviour. Some readers will regard his description of school life as filling the best pages in the book. Traditional conventions of schoolmasters and teachers of English are blown to pieces with a gusty and convincing reality, and the ambitions and frustrations of the boy at puberty and adolescence are expounded with a realism which is never repellent. Human life at all ages comes in for shrewd analysis with detachment from prejudice.

Ellery did himself harm by his advocacy of Communism; he visited Russia and found, as he thought, a well-ordered, progressive, efficient and happy society founded on Marxian principles. When in argument he was confronted with police tyranny, purges, labour camps, controlled science and expurgated news of other countries, his reply was that the end justifies the means—a very dangerous doctrine. There is evidence that Ellery in the latter part of his life entertained doubts about the certainty of these convictions.

The style is vigorous and colourful. Some fastidious critics may think that there is too much use made of quotations; others that he was over-addicted to the device of consonantal alliteration. These are small matters and do not detract from the literary merits of his writing. His references to the progressive arthritis which crippled him and to the malignant antrum which proved fatal are presented with a calm courage unalloyed with self-pity. The claims of this autobiography to be regarded as a work of literary distinction must be taken seriously. A tribute should be paid to the publisher for the high quality of paper, printing and binding and the general attractive appearance of the book.

The Year Book of Drug Therapy (1955-1956 Year Book Series). Edited by Harry Beckman, M.D.; 1956. Chicago: The Year Book Publishers, Incorporated. 7¾" × 5", pp. 560, with 64 illustrations. Price: $6.00.

THE introduction to this Year Book, as usual, provides a swift and comprehensive survey of the year's main contributions in the field of drug therapy; then follow relevant abstracts taken from a wide range of medical literature. They are grouped into sections dealing with allergy, antibiotics and sulphonamides, cardio-vascular diseases, dermatology, endocrinology, gastro-enterology, hæmatology, internal medicine, neuropsychiatry, obstetrics and gynæcology, ophthalmology, oto-rhino-laryngology, pædiatrics, surgery and venereology. The section on cardio-vascular diseases is further divided into subsections on arrhythmias, congestive heart failure, coronary disease, hypertension, miscellaneous entities, peripheral vascular diseases and thrombosis, thrombophlebitis and the anticoagulant drugs. The subdivisions of the section on internal medicine deal with infectious diseases, kidney disturbances, liver disorders, neoplastic diseases, chest diseases, *diabetes mellitus*, pain, poisoning, rheumatic disorders, thyrotoxicosis, and worms and flukes. These sectional and subsectional headings will indicate the almost universal appeal of this book to the medical profession. It should provide a useful and discriminating guide to the bewildering array of new therapeutic methods and drugs which appear each year.

Neural Control of the Pituitary Gland. By G. W. Harris, F.R.S., Sc.D., M.D.; 1955. London: Edward Arnold (Publishers), Limited. 8½" × 5½", pp. 297, with illustrations. Price: 30s.

PROFESSOR HARRIS'S monograph on the pituitary is the third of a series published under the ægis of the Physiological Society of Great Britain. It is the purpose of these monographs to bring together in one volume various aspects of a subject to which the author has himself made important contributions.

The scope of the subject matter to be dealt with is clearly defined in an introductory chapter and is far wider than might be imagined from the title of the monograph. The latter could well have been "The Neural Control of the Endocrine Glands". We are reminded that "the central nervous system is largely responsible for correlating endocrine activity with that of the other systems of the body, and with the varying requirements of the organism due to environmental change". The greater part of the monograph is "an attempt to analyse the mechanism by which the central nervous system, and the hypothalamus in particular, controls and integrates the activity of these glands". The central thesis is that only the neurohypophysis and adrenal medulla have a secreto-motor nerve supply and that the thyroid, adrenal cortex and gonads are brought under nervous control through the mediation of the adenohypophysis. For this reason it is not surprising that, although the discussion ranges widely over the whole field, the dominant problem throughout the first seven of the thirteen chapters in this book should relate to the nature of the hypothalamic control over adenohypophyseal activity. For some years now Professor Harris has been the chief proponent of the view that this control is mediated by some stimulus, probably humoral in nature, transmitted from the hypothalamus along the hypophyseal portal system of blood vessels. The evidence for this view is certainly formidable and has been very ably put forward here. It is difficult to avoid the conclusion that the portal vessels are an essential link, but the nature and site of production of the supposed humoral agent remains obscure. Professor Harris suggests that nerve fibres in the hypothalamus liberate a substance into the primary plexus of the portal vessels.

Five chapters are devoted to the neurohypophysis. The hypothesis that the posterior lobe hormones have a neurosecretory origin still lacks satisfactory experimental support.

A final chapter broadens the discussion in a manner indicated by its title, "Hormones and Behaviour".

The book has been written primarily for the advanced student in physiology, but it can be thoroughly recommended to anyone interested in this general field.

Cardiovascular Innervation. By G. A. G. Mitchell, O.B.E., T.D., M.B., Ch.M., D.Sc., with a foreword by Sir Geoffrey Jefferson, C.B.E., M.S., M.Ch., M.Sc., LL.D., F.R.C.P., F.R.C.S., F.R.C.S.I., F.R.F.P.S., F.A.C.S., F.R.S.; 1956. Edinburgh and London: E. and S. Livingstone Limited. 9¾" × 7", pp. 368, with many illustrations. Price: 55s.

PROFESSOR MITCHELL has quickly followed his "Anatomy of the Autonomic Nervous System" with this volume, ostensibly restricted to the problem of cardio-vascular innervation. In fact, the scope of the book is very much wider than the title implies, since there is a complete survey of the whole anatomy and some of the physiology of the autonomic nervous system as well. This would be admirable but for the fact that the author has just produced a sizeable volume specifically for that purpose. Under the circumstances a more modest monograph relating strictly to the matter in hand would have proved less irksome to busy people seeking detailed information quickly. As it stands, the book provides a useful compilation of information—but not much of it immediately relevant to cardio-vascular innervation (for example, differences of opinion on the arrangement of the oculomotor nucleus)—gathered from a wide range of sources. Indeed, the author betrays an extensive knowledge of neurological literature and concludes with an enormous bibliography—*à l'américaine*—which still, however, manages to miss some important papers. The numerous illustrations are generally good, but some contain too much detail for easy reference. On the whole, and despite some typographical errors, the presentation is satisfactory.

Microbiology: With Applications to Nursing. By Catherine Jones Witton, M.A.; Second Edition; 1956. New York, Toronto, London: The Blakiston Division, McGraw-Hill Book Company, Incorporated. 9" × 6", with many illustrations; pp. 634. Price: $6.00.

THIS remarkably comprehensive account of microbiology is one of the McGraw-Hill Series in Nursing. The dust-cover refers to it as "a scientific and comprehensive text presenting microbiology as a tool for professional use". It is remarkably well and sensibly written, and covers the whole wide realm of its subject, and even extends beyond protozoology to include such macroscopic parasites as tapeworms and flukes. It can hardly be intended as a text-book for nurses during their training, but it is an admirable volume to be placed in the nurses' library for frequent consultation. For instance, when the nurse is told about viruses, she can here read a detailed account of them and of their properties and see admirable illustrations of them taken by the electron microscope. The volume, in fact, is one that can be read with interest and indeed much satisfaction by many a medical man, to bring him broadly up to date with the rapidly advancing knowledge of a now very complicated subject.

The contents of some of the chapters will indicate the wide scope of the subject matter. Thus Chapter II deals with the morphology of the bacteria, including that revealed by electron micrography; Chapter IV deals with their physiology; and other chapters deal with the microscope including the electron microscope, with non-medical microbiology, with sterilization, disinfection and detergents, and with chemotherapy. Part III discusses the sources and modes of infection; Part IV is on infection and immunity, including allergy; Part V is an introduction to the study of the pathogens, commencing with a chapter on the history of microbiology; Part VI is on the pathogenic bacteria; and Part VII on the rickettsiæ, the viruses, the actinomycetes

and fungi. There is even a chapter on the pathogenic protozoa and a short one on worms. Apart from works cited at the end of each chapter, Appendix A gives some of the literature on microbiology. Appendix B classifies the medically important Schizomycetes.

A volume of 400 pages for nurses! "But still the wonder grew, that one small head could carry all she knew." This is an admirable book for consultation by the nurse and quite a good one for the doctor. It is a book that the general practitioner, and even the consultant, may find a useful "tool for professional use". We recommend it.

The Year Book of Orthopedics and Traumatic Surgery (1955-1956 Year Book Series). Edited by Edward L. Compere, M.C., F.A.C.S., F.I.C.S.; 1956. Chicago: The Year Book Publishers, Incorporated. 7½" x 5", pp. 333, with many illustrations. Price: $6.50.

THIS Year Book is, as previously, edited by Edward L. Compere, who in the introduction briefly comments on some points which have arisen in the orthopædic and traumatic field in the last year. He states that during 1955 the orthopædic emphasis has changed somewhat in the treatment of injuries to the cervical part of the spine, arthroplasty of the hip, and operation for the relief of backache with sciatic nerve pain. There has been no revolutionary new discovery in orthopædic surgery as a specialty. The editor refers to the Salk vaccine, which he states has been declared to be about 80% effective. He also comments on the increasing incidence of whiplash injuries, and makes recommendations as to their treatment.

The subjects dealt with in this Year Book are the same as in the previous volume, except that a section has been added on calcium and phosphorus metabolic diseases of bone. The illustrations are numerous and, as usual, of good quality. The book is, also as usual, a valuable compendium of the latest information in this specialized field.

Atlas of Tumor Pathology (Washington: Armed Forces Institute of Pathology). Section III—Fascicle 7: "Tumors of the Cardiovascular System", by Benjamin H. Landing, M.D., and Sidney Farber, M.D.; 1956. 10½" x 8", pp. 138, with 138 illustrations. Price: $1.50. Section V—Fascicle 19: "Tumors of the Thymus Gland", by Benjamin Castleman, M.D.; 1955. 10½" x 8", pp. 82, with 85 illustrations. Price: $1.00. Section IX—Fascicle 33: "Tumors of the Female Sex Organs." Part I: "Hydatidiform Mole and Choriocarcinoma", by Arthur T. Hertig, M.D., and Hazel Mansell, M.B., B.S.; 1956. 10½" x 8", pp. 63, with 65 illustrations. Price: $1.00.

THE seventh fascicle of Section III of the "Atlas of Tumor Pathology", issued by the Armed Forces Institute of Pathology of the United States, provides some magnificent reproductions of pictures of tumours and of their histological sections. It is impossible to imagine finer reproductions. The fascicle is divided into several sections dealing respectively with tumours of the pericardium, tumours of the heart, tumours of the blood vessels and tumours of the lymphatic vessels. The authors, Benjamin H. Landing and Sidney Farber, point out that the cardio-vascular system is a common source of benign tumours, but a relatively rare source of malignant tumours. Tumours of the heart tend to appear in well-defined types. On the other hand, tumours of the blood vessels and to a lesser extent those of the lymphatic vessels are less well defined and are subject to wider speculations. Thus the American Cancer Society has a list of tumour diagnoses which records 224 terms for tumours of this group exclusive of those of specialized vascular structures, angiomatous forms of other tumours and Ewing's tumour. The authors have classified the tumours which they describe primarily on the basis of microscopic appearance. A table is given in which the tumours and tumour-like lesions of the heart are set out. The primary tumours of the heart described and illustrated include myxoma, hæmangioma and lymphangioma, rhabdomyoma, fibroma, lipoma and hamartoma, miscellaneous tumour-like lesions, and sarcoma. Metastatic tumours of the heart are also illustrated. Of the tumours of the blood vessels, benign lesions and malignant lesions are illustrated. The benign lesions include hemangiomata, hamartomatous angiomatoses, and malformations. The malignant lesions include angiosarcoma, Kaposi's sarcoma, sarcoma arising in hæmangioma, lesions confused with angiosarcoma and malignant tumours arising in the walls of blood vessels. Under tumours of the lymphatic vessels various groups of lymphangiomata are described.

Fascicle 19 of Section V deals with tumours of the thymus gland and the author is Benjamin Castleman. There is an introduction and then come sections on thymoma, tumours resembling thymoma and other tumours of the thymus gland. Some of the illustrations in this fascicle are in colour and the reproduction leaves nothing to be desired.

Fascicle 33 of Section IX deals with tumours of the female sex organs. Only Part I of this fascicle has been forwarded. It deals with hydatidiform mole and choriocarcinoma. The authors are Arthur T. Hertig and Hazel Mansell. They have an interesting introduction on pathogenesis of the hydatidiform mole and on the histogenesis of trophoblast. They discuss the latter in its relationship to hydatidiform mole and choriocarcinoma. Some of the illustrations in this fascicle are in colour, but pride of place in this fascicle must be given to the black and white illustrations.

This magnificent tumour atlas must surely be the envy of every place where pathology is taught. The sheets are assembled for loose leaf binding in such a way that they can easily be separated and used in a projection apparatus. To congratulate those who are responsible for the production of this work seems almost to be an impertinence.

The Year Book of Dermatology and Syphilology (1955-1956 Year Book Series). Edited by Rudolf L. Baer, M.D., and Victor H. Witten, M.D.; 1956. Chicago: The Year Book Publishers, Incorporated. 7½" x 5", pp. 480, with many illustrations. Price: $6.50.

THIS Year Book of Dermatology and Syphilology is the first in twenty-four years of which Marion B. Sulzberger does not share the editorship. Dr. Sulzberger has now retired from his editorial position; Rudolf L. Baer has become the senior editor in his place, and the junior position is filled by Victor H. Witten. The new editorial team pays a graceful tribute to Dr. Sulzberger's work.

In their introduction the editors comment on various lines of research, amongst which the following may be noted: studies on cutaneous enzymes, outstanding among them being the work of Shelley and Arthur on the role of endopeptidases in itching; lipid metabolism (of importance not only in dermatology, but also possibly in relation to arteriosclerosis); the technique of surface "stripping" of the skin, and the avenues which it opens up; work on the various dermatoses; and so on. Attention is also drawn to the treatment of large body areas with forms of radiation which, although they are extremely effective on the skin lesions, have little effect on underlying structures. The editors refer to the reports on systemic and topical treatment, particularly those relating to corticosteroids and their newer analogues. A warning is given that the topical application of 9-α-fluorohydrocortisone, which has a much greater anti-inflammatory action than hydrocortisone, has been proved to carry a risk of producing disturbances in water and electrolyte balance.

This Year Book deals with articles published in journals received from December, 1954, to the end of November, 1955. The material is arranged under headings which do not differ greatly from those employed in the 1954-1955 edition. The editors' final comment adequately sums up the reader's impression of the present position of dermatology: "This year's literature once more testifies to the fact that the era of interest centered mainly on the descriptive and morphologic aspects of skin diseases has faded into the distant past and that the current advances in dermatology are keeping a steady pace with the remarkable progress of medicine in general."

Methods of Biochemical Analysis. Edited by David Glick; 1956. New York: Interscience Publishers, Incorporated. London: Interscience Publishers, Incorporated. Volume III. 9" x 6", pp. 447. Price: $9.50.

ANNUAL review volumes dealing with different fields in science have proved themselves of great value to research workers and others. Most of them have been concerned primarily with results. Interscience Publishers, Incorporated, who produce many of these review volumes, are now running a series giving details of the latest technical methods for use in biochemical analysis. The third annual volume has just appeared under the editorship of David Glick. Twenty-three contributors, all active workers in their respective fields, have presented twelve articles on various aspects of biochemical analysis. The ground covered is extensive and includes determination of organic phosphorus compounds, determination of histamine, enzymic microdetermination of uric acid and other purines, periodic oxidations, end group analysis of polysaccharides, measurement of complex ion stability, analysis of metal protein complexes, and determination of zinc in biological materials. The book is essentially one for the research laboratory. Some of the

articles contain a good deal of theoretical discussion, but are mostly concerned with technical details.

The book should be very useful in a biochemical research laboratory, but has little that would appeal to workers in medical biochemistry.

The Princes in the Tower and Other Royal Mysteries. By Sir Arthur Salusbury MacNalty, K.C.B., M.A., M.D. (Oxon.), F.R.C.P., F.R.C.S.; 1955. London: Christopher Johnson. 8¼" x 5½", pp. 212. Price: 18s.

MORE than thirty years ago, an Australian surgeon published a number of scholarly essays recalling historical episodes in the lives of certain royal personages who had managed to leave a lasting imprint on the scroll of time. They were written in a convincing and most attractive style, and were noteworthy for the novel interpretations of physical weakness, abnormal behaviour or mode of death in his characters as seen by the trained eye of a medical man. Since those days a number of similar studies have been undertaken by doctors well qualified to write on such topics by reason of some special knowledge in the fields of both history and medicine.

More or less in the same strain, Sir Arthur S. MacNalty, in his book "The Princes in the Tower", discourses on the character and behaviour of several historical personages belonging to European royal families, and gives his own interpretation of the deep mystery which still surrounds a certain event in the life or death of the principal character. Readers with an historical bent will find much to interest them in these pages; although they may be disappointed to find that the young princes mentioned in the title are disposed of in a very short chapter at the beginning, and that subsequent attempts to clear up this famous murder mystery have done nothing to mitigate the evil reputation of King Richard the Third.

With the exception of the next two chapters, which are too involved and overburdened with the wicked deeds of Spanish royalty in the sixteenth century, the remaining narratives all have a compelling interest in spite of a studied economy in the use of quiet humour and poetic licence. However, these subtle qualities are inherent in the amazing story of Sophy Dawes, the illegitimate daughter of a drunken fisherman from the Isle of Wight, who with more than her share of physical attraction, loose morals and feminine charm, succeeded in realizing a youthful determination to rise above her lowly station in life and move about in high society. Unhampered by any qualms of conscience, she used her natural talents to attain wealth and influence at the French Court as the faithful mistress of an aging Duke of Bourbon, who later, for the sake of social respectability, arranged her marriage with the guileless Baron de Fuchères.

These essays, besides having an entertainment value, provide ample justification for the revolutionary democratic movements of the early nineteenth century to bring about political and social reform.

History of the Second World War: United Kingdom Medical Series. Editor-in-Chief, Sir Arthur S. MacNalty, K.C.B., M.A., M.D., F.R.C.P., F.R.C.S. **The Royal Air Force Medical Services.** Edited by S. C. Rexford-Welch, M.A., M.R.C.S., L.R.C.P., R.A.F. Volume II: Commands. 1955. London: Her Majesty's Stationery Office. 9½" x 6", pp. 727, with many illustrations. Price: £3 15s.

VOLUME I of this series relating to the Royal Air Force dealt very comprehensively with the general problems of administration. This volume discusses in detail the activities of the fighter, bomber, and other commands which were many and varied and have both general and technical interest.

The development of aviation medicine during the war is again discussed, and in particular, problems of anoxia and its prevention with special reference to the training of personnel. Modifications of oxygen installations in aircraft must of necessity keep pace with mechanical and structural improvements necessitated by constant demands for increased performance in high speed and altitude flying. To the ultimate development of an efficient oxygen mask facepiece and microphone the Royal Air Force Physiological Laboratory made an important contribution. Specialist medical assistance was also available in improving methods of dark adaptation and night visual training generally.

A most important and helpful innovation was the appointment of flying personnel medical officers, whose duty it was to investigate all factors affecting functional or occupational efficiency of flying personnel, to inspect all equipment used in so far as it involved medical and physiological aspects, and in particular to study any factors predisposing to non-effectiveness in flying personnel. They were able to keep laboratory and research workers in touch with the rapid development in the practical side of flying. Those officers were carefully selected and were from the outset most successful. Many of them had already had flying experience which was found to be essential for a complete understanding of air crew problems. They are given credit not only for increasing the safety and comfort of the crews, but also for having definitely contributed to the successful prosecution of the war.

With so many problems common to most of the commands, it is inevitable that in this book there should be some overlapping and repetition, but this has been kept at a minimum by careful planning.

Each command had also its own peculiar problems. The frequency of accidents in parachute training, the organization of sea and mountain rescue services, ophthalmic difficulties from the extended use of radar, the problem of yellow fever control in transport command, first-aid treatment in damaged aircraft, investigation of factors influencing "flying stress", difficulties in water supply and conservancy in remote locations such as Iceland—these are merely a few of the problems which might lend variety to the tour of duty of the medical officer of the Royal Air Force.

The editor has been fortunate in his collaborators, who write with authority and intimate knowledge derived from first-hand experience which greatly enhance the value and importance of the "History".

Atlas of Plaster Cast Techniques. By E. E. Bleck, M.D., Nellie Duckworth and Nancy Hunter; 1956. Chicago: The Year Book Publishers, Incorporated. 9½" x 6½", with 347 illustrations. Pp. 128.

THIS is a small book devoted to the practical details of plaster of Paris technique. It is intended primarily for the help of inexperienced operators, but senior people might easily pick up a worthwhile point from it. The various procedures are described in steps, with photographs or diagrams illustrating each stage. More than half of the book is in illustrations, and these are clear and to the point. It should be possible for anyone to follow the technique set out. Though small, the book describes all the common casts, and in many instances alternative methods are also given. One feature is the ring-back binding, which enables the book to lie flat at any opening.

This atlas should be of great use in plaster rooms, or for reference where plaster work must be carried out, although infrequently.

Gynecologic Cancer. By James A. Corscaden, Ph.B., M.D.; Second Edition; 1956. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" x 6", pp. 553, with illustrations. Price: £5 10s.

"GYNECOLOGIC CANCER", in its second edition, carries all the excellence of the first edition and incorporates the advances of the last four years. This is a most optimistic treatise on such a grim subject, because stress is laid on the curability of the disease. It is indeed a fact that too much of the darker side is obvious to the laity, the student and the young intern. The patients cured are never obviously presented in public, and the author has gone so far as to design a button to be worn by members of a "Cured Cancer" Club.

Prognosis is in direct ratio to early diagnosis, and a large section of the book is taken up with this, including routine examination for female patients over thirty years of age. It is pointed out that delay in diagnosis was the fault of the physician in 27% of the author's cases. Gynæcological cancer is an accessible cancer, and vast improvements can be effected in the results if the family doctor will remember that not looking is far more blameworthy than not knowing.

For the specialist engaged in treatment of this cancer, a detailed portion of the book is devoted to lesions of the various gynæcological organs. Classification follows international standards, and a strong case is made out for the inclusion of a lesion deserving of a special designation, cancer *in situ*, pre-invasive cancer *et cetera* as a true cancer localized in the epithelial layer.

In operative treatment of cancer of the cervix, technical details are included for a true radical hysterectomy. If irradiation is to be used, the author discusses the Manchester, Stockholm, Curie and other techniques and includes a description of his own applicator. In cancer of the cervix,

the author concludes that the best irradiation techniques give about the same five-year survival rates as the best operative techniques. Radioactive isotopes and X-ray therapy of higher voltage are evaluated and described. Each chapter ends with an excellent list of available references.

The personal patient approach is emphasized by short chapters, which conclude the book, on the menopause and the management of the cancer patient. Many misconceptions are pointed out, such as the association of arthritis or hypertension with the menopause, and the treatment of psychic disorders at this time with œstrogens is labelled as highly dangerous.

In the management of the cancer patient, the most important problem is, should she be told the truth? The author considers that she should in answer to a direct question, but that treatment only and not diagnosis should be discussed otherwise. When the woman of today was young, "cancer" was regarded as a death sentence, but now the physician can promise well towards 90% cure of cancer of the skin, rectum, breast and uterus.

The final few pages are given over to speculation as to the nature of cancer.

One finishes reading this large book, beautifully produced and printed, with a sense of having covered the subject of gynæcological cancer in as full a manner as is known today. At the same time, there is a feeling of cheerfulness, but not of apathy, because of the advances made and the rising cure rate, on which, in this optimistic treatise, accent is always placed. Anyone remotely connected with the subject matter should possess this book.

Food Poisoning. By G. M. Dack, Ph.D., M.D.; Third Edition; 1956. Chicago: The University of Chicago Press. 9″ × 6″, pp. 262. Price: $6.00.

THIS book gives a complete and concise account of illnesses caused by poisons or organisms in food.

The first chapter outlines methods of investigating an outbreak of suspected food poisoning and gives a résumé of useful points for differentiating the causative agents.

In subsequent chapters a more complete account is given of specific causes. These are grouped under the headings of chemical poisons, poisonous plants and animals, botulism, staphylococcus food poisoning, salmonella food poisoning, *Streptococcus fæcalis* in relation to food poisoning, and food poisoning due to other bacteria. The last chapter deals with differentiation of infections from food poisoning. Each cause is discussed under headings dealing generally with information of historical interest, epidemiology, symptoms, treatment, laboratory diagnosis and control. Special aspects of each cause are also considered. A large number of references, many as recent as 1954, are given at the end of each chapter.

Many tables which briefly summarize facts given in the text are included. These are useful for quick reference.

In the chapter on chemical poisons only common chemical poisons associated with food or those which produce symptoms similar to microbial poisoning are considered.

The chapter on poisonous plants and animals is of interest, if not of great practical value.

The chapters on poisoning by bacterial toxins are probably of more value to Australian practitioners. Descriptions of actual outbreaks of food poisoning add interest to the text.

The book is written and printed in a manner that makes it easy to read. It should prove to be a useful reference book for bacteriologists and general practitioners and a valuable text-book for medical officers specializing in preventive medicine.

Notes on Books, Current Journals and New Appliances.

1956 Medical Progress: A Review of Medical Advances during 1955. Edited by Morris Fishbein, M.D.; 1956. New York, Toronto and London: The Blakiston Division of the McGraw-Hill Book Company, Incorporated. 9″ × 6″, pp. 390. Price:

ANY book edited by Morris Fishbein is certain to attract attention. This review of medical advances during 1955 cannot therefore be passed by. The chapter subjects range from general medicine to general surgery, from ophthalmology to orthopædic surgery, and include such matters as poliomyelitis vaccine, nutrition, psychiatry and new drugs; there are 21 chapters in all. Fishbein informs us in his preface that the fields covered in the current volume are the same in subjects and author as those in previous volumes, but that sometimes subjects and authors have been changed to bring new points of view and new emphases. This work should be of interest to those who like reviews of this kind.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"An Introduction to Electrocardiography", by L. Schamroth, M.B., B.Ch. (Rand), M.R.C.P.E., F.R.F.P.S.; 1956. Cape Town and Johannesburg: Juta and Company, Limited. 9½″ × 6″, pp. 72, with illustrations. Price: 21s.

This book is intended to be a "stepping-stone" to the fuller and more detailed study of the subject.

"Ciba Foundation Colloquia on Endocrinology"; Volume IX: "Internal Secretions of the Pancreas"; editors for the Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Cecilia M. O'Connor, B.Sc.; 1956. London: J. and A. Churchill, Limited. 8″ × 5″, pp. 314, with 100 illustrations. Price: 40s.

Consists of papers and discussions on fifteen subjects.

"Meditations on Medicine and Medical Education: Past and Present", by I. Snapper, M.D.; 1956. New York and London: Grune and Stratton. 8½″ × 5½″, pp. 144. Price: $3.75.

Deals with New Netherland under the Dutch and the influence of Boerhaave, of Leyden, on medicine in the United States of America.

"Medical Bacteriology: Including Elementary Mycology and Parasitology", by Sir Lionel Whitby, C.V.O., M.A., M.D. (Camb.), F.R.C.P. (Lond.), D.P.H., and Martin Hynes, M.D. (Camb.), M.R.C.P. (Lond.); Sixth Edition; 1956. London: J. and A. Churchill, Limited. 8″ × 5″, pp. 548, with 103 illustrations. Price: 30s.

The first edition was published in 1928.

"Progress in Psychotherapy, 1956", edited by Frieda Fromm-Reichmann, M.D., and J. L. Moreno, M.D.; 1956. New York and London: Grune and Stratton. 9″ × 6″, pp. 363. Price: $8.50.

This book is "closely linked to the development of the Section on Psychotherapy within the American Psychiatric Association".

"A New Psychotherapy in Schizophrenia: Relief of Frustrations by Symbolic Realization", by Marguerite Sechehaye, translated by Grace Rubin-Rabson, Ph.D.; 1956. New York and London: Grune and Stratton. 8½″ × 5½″, pp. 206. Price: $4.50.

Lectures delivered at the Bürgholzli Psychiatric Clinic in Switzerland

"Treatment of the Child in Emotional Conflict", by Hyman S. Lippman, M.D.; 1956. New York, London, Toronto: McGraw-Hill Book Company, Incorporated. 8½″ × 6″, pp. 308. Price: $6.00.

The methods described are based on instruction received in the seminars of Anna Freud and August Aichhorn.

"Modern Gynæcology with Obstetrics for Nurses", by W. E. Hector and John Howkins, M.D., F.R.C.S.; 1956. London: William Heinemann (Medical Books), Limited. 8½″ × 5½″, pp. 211, with illustrations. Price: 17s. 6d.

Emphasis is placed on the role of the nurse in gynæcological wards.

"Oral Cancer and Tumors of the Jaws", by George S. Sharp, M.D., F.A.C.S., F.A.C.R. (Ther.), Weldon K. Bullock, M.D., M.Sc. (Path.), and John W. Hazlet, D.D.S.; 1956. New York, Toronto, London: McGraw-Hill Book Company, Incorporated. 9″ × 6″, pp. 572, with illustrations. Price: $15.00.

The purpose of the book is to provide a manual for the recognition of oral cancer, to illustrate with text and photographs the difference between benign and malignant tumours, and to be of help in diagnosis before a biopsy specimen is taken.

The Medical Journal of Australia

SATURDAY, SEPTEMBER 29, 1956.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE INEQUALITY OF MEN.

THE American Declaration of Independence, proclaimed on July 4, 1776, is one of the world's famous documents, and perhaps its most famous passage is the statement of the equality of men:

> We hold these truths to be self-evident, that all men are created equal; that they are endowed by their Creator with inalienable rights; that among these are life, liberty and the pursuit of happiness.

Thomas Jefferson, who drew up the Declaration, could not persuade Congress to accept everything in his original draft (notably his denunciation of the slave trade and recommendations for the abolition of slavery), but he did get them to agree officially (even if inconsistently) with his idea of the equality of men; and his thoughts have been echoed and his words quoted ever since. It would surely have dismayed him if he had known that nearly two centuries later a famous namesake, the neurologist Sir Geoffrey Jefferson,[1] would state that the idea had been adopted and written into the Declaration "by men moved more by emotion than by common sense" and would make the further assertion:

> No man today will hold that all men are born equal in anything but impotence, whatever their political rights may be, though even there we would well guess that some men and some peoples would use them with greater wisdom than others.

This is a trifle sweeping, especially the phrase "No man today will hold", for the United Nations Declaration of Human Rights, prepared in 1948, states:

> All human beings are born free and equal in dignity and rights. They are endowed with reason and conscience and should act towards one another in a spirit of brotherhood.

[1] *Lancet*, November 5, 1955.

Is this yet another statement by "men moved more by emotion than by common sense"? Was T. H. Huxley right when (as Sir Geoffrey Jefferson tells us) he called the equality of men "probably the most astonishing falsity that ever was put forward by a political speculator"?

A little reflection suggests that the conflict is more apparent than real. It seems to be an argument at cross purposes, arising inevitably from the use of generalizations. The inequalities of men in many important respects are obvious, although they have been curiously overlooked at times. Sir Geoffrey Jefferson refers to the great efforts made by "intelligent, influential and generous men and women" in the last century towards the education of "the working classes", based on the idea that the differences between men were the result of ignorance and not of differing capacity. These crusaders sought to set society aright by education, labouring "in the hope, let us suppose" (Sir Geoffrey Jefferson writes a little cynically), "that the workers would think exactly the same way as their educational benefactors". They were unfortunately pursuing an illusion. The fact, as most people will agree, is that the capacity of individuals to absorb and use information varies widely. Men are not equal in intellect, or in most other functions of mind and body; nor, it would seem, are they born equal in these things. True, the role of inheritance in determining the capacities, physical and mental, of any individual is still debated and cannot be finally determined without more data; but the point of inherent inequality is sufficiently proved, even if reduced to the ridiculous, by comparison of the normal child with the microcephalic idiot or with the child suffering from a gross congenital cardiac defect.

Granted that certain inequalities occur, we must decide how to regard them. Some can be dismissed as unimportant; some have far-reaching effects; some, perhaps most, are assessed variously in importance according to time and circumstances. What is always important is that inequality does not warrant emotionally coloured attitudes of superiority and inferiority. There is nothing praiseworthy in being born with mental or physical attributes that are advantageous or particularly acceptable in society. Nor should the reverse be a matter of shame. Hans Christian Andersen remarks, in his story "The Ugly Duckling", "It does not matter in the least having been born in a duckyard, if only you come out of a swan's egg!"; but in practice you usually need to be among the swans to find life tolerable. Mutual contempt or self-sufficient pity is common between the mentally dull athlete and the scholar who is clumsy at games, the penniless artist and the commercially successful Philistine, the coloured man and the white, the Oriental and the Westerner. Yet neither is strictly rational in his attitude, and both would be better employed learning from the other. The old proverb "You cannot make a silk purse out of a sow's ear" is true but lopsided in its usually accepted implications. We forget that the sow (worthy creature) cherishes her ears, but has neither use nor regard for a silk purse.

Part of the trouble seems to lie in confusing genuine inequalities with mere differences—things like colour, race, social standing and group outlook, which for various reasons, mostly emotional, have been allowed to divide men. Inequalities of endowment occur between individuals of different groups and between individuals of the same

group, but it is a fallacy to classify an individual according to a general impression (whether true or false) of his whole group. In the matter of the genuine inequalities we do well to ponder the words of A. F. Alford,[1] Senior Medical Officer in the British Ministry of Education:

> The point to be driven home to the public at large, as well as parents, is that every child who is handicapped either in mind or body should be looked upon not as a defective but as a normal child, with a deviation from normality in one particular respect. This positive approach tends to focus attention on potentialities instead of imperfections.

In addition, it eliminates from this field the conceptions of superiority and inferiority, tangled up as they are with ideas of contempt, dominance, envy and self-pity—all of them damaging to human dignity and self-respect. This is not just a matter of political or personal opinion, outside our professional sphere; it is intensely practical. As Alford points out, the retarded child must have within him a sense of self-respect if his mental health is to flourish. Many factors go towards this—uninhibited mother love and good family relationships, full development of intellectual powers leading to achievements both in thought and in action, fostering of independence, belief in and realization of innate abilities, and, above all, acceptance by others. Mentally retarded children must be aided to "live a full life within their limitations, giving them a sense of satisfaction, worth, and usefulness". This can come, not only in relation to such children, but in other respects, only as we abandon the idea that inequalities, mental or physical, make some people "better" or "worse" than others. As William C. Boyd[2] has written, before we decide that some human beings are better than others, we must ask ourselves: "Better for what?"

> It is not easy to say with confidence that any of the varieties of ability are bad, and others are good, or that some are better than others. Was Sir Isaac Newton more valuable to the human race than Ludwig van Beethoven? This question cannot be answered scientifically because it is a silly question and has no meaning, and nearly all similar questions which involve the ideas of good and bad in human abilities are equally silly.

We have still to consider in what sense, if any, all men are born equal, although a good deal of the answer to the question has been implied in what has been written. It needs to be appreciated that Huxley, whom Sir Geoffrey Jefferson has quoted so approvingly, was largely attacking a strawman—in other words, certain of the highly vulnerable speculations of Jean-Jacques Rousseau. Rousseau undoubtedly influenced his contemporaries to a surprising degree, and his theories played a real part in stimulating the French and American Revolutions; but his discredited views on the noble savage have little in common with what Thomas Jefferson and the United Nations Declaration are concerned with. The claims to equality in "dignity and rights", the rights to "life, liberty and the pursuit of happiness", are real and vital. They are not to be brushed aside with a parenthetical "whatever their political rights may be". These are not "political rights". They are bound up with any adequate concept of the worth of human personality. They form a universal birthright that no man should be able to take from another. At the same time they can be forfeited; and not to labour the point, it is perhaps sufficient here to quote Mahatma Gandhi's words[1] in a letter to the Director-General of UNESCO in 1947:

> I learnt from my illiterate but wise mother that all rights to be deserved and preserved come from duty well done. Thus the very right to live accrues to us only when we do the duty of citizenship of the world. From this one fundamental statement, perhaps, it is easy enough to define the duties of Man and Woman and correlate every right to some corresponding duty to be first performed. Every other right can be shown to be a usurpation hardly worth fighting for.

[1] *Lancet*, June 18, 1955.

[2] "Genetics and the Races of Man: An Introduction to Modern Physical Anthropology" (1950), Blackwell, Oxford, 358.

[1] Quoted in "The Colour Problem: A Study of Racial Relations", by Anthony H. Richmond (1955), Penguin Books, 319.

Current Comment.

PERTUSSIS AND BEHAVIOUR DISORDERS IN CHILDREN.

AN investigation was carried out in the Department of Child Psychiatry at the University Hospital of Uppsala in the three years 1949 to 1951. The report is published in a monograph.[2] The author first presents a body of current opinion on the importance of minor brain damage as a cause of a particular behaviour disorder characterized by unpredictable variations in mood, short attention span, hypermotility, impulsiveness, variable memory, difficulties in speech, reading and arithmetic, slight neurological symptoms, emotional disturbances with anxieties and difficulties in adjustment, and so on. Various acquired factors such as encephalitis, anoxia and trauma are accepted as possible causes of this "lesional syndrome", and pertussis is presumed to be able to cause it either by circulatory disturbances and anoxia during the coughing paroxysms, or perhaps by a specific "whooping cough encephalopathy".

The investigation was planned to decide the ætiological importance or otherwise of pertussis contracted during the first eighteen months of life. The approach was made from two aspects. Firstly, 65 children who gave a history of having had pertussis in infancy were collected from the total number of children under the age of twelve years who attended at the clinic with behaviour disorders of all sorts during the period of the survey. These 65 children were examined for the various manifestations of the "brain-damage syndrome", and were compared with 130 other children who had attended the clinic and had no such previous history of pertussis. A detailed statistical analysis of the differences, symptom by symptom, and then by symptom-complexes, between the two groups, is presented, but the results are not by any means overwhelming support for the thesis.

The second approach was to examine 41 "normal" children with a history of pertussis in infancy, who were selected from an appropriate sample of school children, and to compare them with two control groups of other school children, one group consisting of 41 children with no such history, the other consisting of 46 children who had contracted some other infectious disease in the first eighteen months. Again, a significant difference was considered to be present, the pertussis group showing a higher incidence of neurological symptoms, including disturbances in fine motor function, and various appropriate behaviour disturbances.

The author acknowledges the difficulty of excluding other causative factors besides pertussis in these disorders, and also admits that in many cases of pertussis such consequences do not follow. One might go further and question the reliability of the history of pertussis in many cases—it is not always an easy disease to diagnose in infants, and

[2] "Pertussis in Infancy as a Cause of Behaviour Disorders in Children", by Anna-Lisa Annell, with Statistical Analysis by Elvir Lander, translated from the Swedish by Erica Odelberg; 1953. Uppsala: Almqvist and Wiksells Boktryckeri Aktiebolag. 9" × 6", pp. 222.

the criteria on which the diagnosis was based in most cases in the survey were not stated. Altogether, this painstaking study demonstrates the considerable difficulty in arriving at statistically unassailable conclusions when dealing with a mass of psychiatric data depending so much on personal interpretation. Dr. Annell, however, has concluded that pertussis in infancy was the actual cause of the behaviour disorders in the children studied, especially when "a comparison is made relevant to the mean number of simultaneously occurring symptoms", and that the influence of other factors can be ruled out. She supports her conclusions with 69 detailed case histories.

SYPHILIS AT THE PRESENT DAY.

In the annual report for England and Wales of the Chief Medical Officer[1] of the Ministry of Health for the year 1954 it is noted that the number of new patients suffering from syphilis who attended public clinics fell to a record low level. There was also a decline in the total numbers of cases of the different manifestations of late syphilis and of congenital syphilis. The increasing efficiency of ante-natal care was shown by the increasing numbers of pregnant women under treatment for syphilis and by the fall in the percentage of positive serological findings in pregnant multiparous women from 0·43 to 0·32 in the large urban centres. In passing, it is worthy of note that the position with regard to the other venereal diseases is not so satisfactory and that this is due, it is suggested, to infected immigrants from tropical countries and to visiting seamen. While official notifications of public clinics can do no more than reflect the incidence of venereal diseases, it seems unlikely that syphilis can present the appalling problem revealed by the survey "Operation Streetcar" carried out in Philadelphia in May and June, 1954, by I. L. Schamberg,[2] and quoted by H. Beerman *et alii*.[3] A random section of the population was tested serologically, and of 35,402 persons, 10·7% were found to give reactive or weakly reactive results to the tests. American workers have also expressed concern at the incidence of venereal diseases amongst seamen, and J. Stuart and G. Joyce[4] found that in American merchant seamen 37·9% of the venereal contacts occurred in Japan. In the United States Navy,[5] also quoted by Beerman *et alii*, the incidence of venereal disease increased by 15% over 1953 levels. The rise was accounted for mostly by an increase in gonococcal infections in naval personnel abroad, but non-gonococcal urethritis was particularly common in personnel in the Far East and in the Pacific area. During this time the incidence of non-gonococcal urethritis was also increasing in England and Wales. However, venereal disease is comparatively rare in the younger adult. C. S. Nicol[6] reports that only 3·6% of males with gonococcal infection were under the age of twenty years, while at the same time, of the infected females, 14·3% were in this youngest age group. The problems of draining the infective reservoir of venereal infection are enormous, and like so many other workers, Nicol suggests that particular attention should be paid to merchant seamen, to the reservoir of amateur and professional prostitutes, and to immigrants. He suggests that more intense propaganda is needed, though it must be accepted that sexual promiscuity will remain.

An interesting side point raised several times during the hearing of the United Kingdom Commission which inquired into the changes of the law regarding homosexuality and prostitution, was the impression that homosexuality had at least the quality that its practice was free of venereal infection. However, F. J. G. Jefferiss found that of 1000 consecutive patients with early venereal infection seen at St. Mary's Hospital Clinic, London, 8·4% admitted to homosexual contact, and this is probably a figure considerably lower than the real incidence.[1] Despite the failing public and even governmental interest in the problems of venereal infection, medical research in this connexion continues to be intense. In a review of the recent published material on syphilis alone, H. Beerman *et alii* were able to quote the views and findings expressed in 225 separate papers published in a twelve-month period.

If we accept the inevitability of sexual promiscuity, it remains to be seen if infection of contacts with venereal disease can be prevented. Wartime experience with the sulphonamides, and more recently with the antibiotics, reveals that gonococcal infections can be easily prevented, though these measures are scarcely justifiable. Attention is rightly drawn to the prevention of syphilis. Again, parenterally given penicillin would frequently be effective, but would be quite inappropriate because of the possible modification of the many signs of the active disease. The many years of experience, in both war and peace, by the armed services lend little support to the local use of soaps and ointments after exposure to venereal infection. R. C. Arnold and J. C. Cutler,[3] in experimentally exposed rabbits, found that a wide variety of agents, including various soaps and most antiseptics, proved to be quite ineffective in preventing the passage of the *Spirochæta pallidum*. Sulphonamide applications were effective only when calomel was included, and of the penicillin preparations for parenteral use only procaine penicillin G was effective. However, aqueous solutions of mapharsen with "Orvus" and solutions of fumerane were frequently effective in the prevention of syphilitic infections.

E. W. Thomas[2] suggests that in the treatment of early syphilis the need is for the maintenance of a moderate concentration of penicillin in the blood for at least seven days. A single dosage of 2,400,000 units of benzathine penicillin G should, theoretically, be more than adequate for this requirement, though the injection of this amount may be rather painful. M. L. Niedelman[4] has used the procaine penicillin in oil with aluminium monostearate in the treatment of late latent syphilis and has found it to be quite effective, especially in the younger age groups. The results, judged by the serological tests, were best in patients who had not previously been treated with penicillin. When penicillin cannot be used, oxytetracycline and chlortetracycline are quite effective, and preliminary reports suggest that erythromycin and magnamycin may be even more effective.

G. R. Baler[5] has used oxytetracycline in the treatment of early syphilis in 16 patients. The oxytetracycline was given by the intramuscular route in a dosage of 200 milligrammes twice daily for ten days. Baler suggests that higher dosages should be employed to increase the efficiency of this form of therapy.

M. J. Fiumara, B. Appel, W. Hill and H. Mescon[6] suggest that both syphilis and gonorrhœa are increasing in frequency in America. They report that, according to a United States Public Health Service estimate, there were, at the end of 1955, 2,000,000 people in that country with syphilis requiring treatment. During 1955 approximately 86,000 new cases of syphilis occurred among the civilian population, a figure enormously in excess of the rates reported by the British survey. Fiumara *et alii*[7] consider that most patients with doubtful fluctuating serological reactions do, in fact, have syphilis.

I. L. Schamberg[8] suggests that only immunization against syphilis can protect the population against the ever-present possibility of a future epidemic of the disease, despite the continued decline in the attack rate of recent years.

[1] *Brit. J. Vener. Dis.*, March, 1956.
[2] *Pennsylvania M. J.*, December, 1954.
[3] *Arch. Int. Med.*, February, 1956.
[4] *Pub. Health Rep.*, December, 1954.
[5] *Stat. Navy Med.*, October, 1954.
[6] *Brit. J. Vener. Dis.*, March, 1956.

[1] *Brit. J. Vener. Dis.*, March, 1956.
[2] *Brit. J. Vener. Dis.*, March, 1956.
[3] *New York State J. Med.*, June 15, 1956.
[4] *Arch. Dermat.*, May, 1956.
[5] *Arch. Dermat.*, May, 1956.
[6] *New England J. Med.*, June 14, 1956.
[7] *New England J. Med.*, June 21, 1956.
[8] *Arch. Dermat.*, May, 1956.

A. W. Stillians[1] emphasizes that if neurosyphilis is to be successfully eradicated, more efficient use must be made of penicillin in the treatment of early syphilis. Further, young people should be educated to help in the whole problem of syphilis, and prostitution and alcoholism should be combated.

It seems likely that the late manifestations of syphilis will continue to be seen for many years. Many syphilitic diseases contracted during the war and untreated may soon be seen in their later stages as the years pass. O. Kofman[2] believes that the best guide to the effectiveness of penicillin in cases of neurosyphilis is the regression in abnormalities of the cerebro-spinal fluid, particularly the cell count and the total protein estimation. The other changes are less reliable. Even so, relapse may still occur up to three years after treatment by penicillin. Like several recent authors, Kofman has not found the Herxheimer response to cause any major side effects in the initial therapy by large doses of penicillin.

W. D. Nicol[3] suggests that the potential dangers of the Herxheimer reaction no longer call for the precautions in building up the full penicillin therapy. However, patients should be investigated for the possibility of penicillin sensitivity. Nicol still believes that the method of choice, at least in parenchymatous neurosyphilis, is to combine malarial therapy with penicillin.

It is now fifty years since August von Wassermann and his associates perfected the reliable serological test for the detection of infection by the *Treponema pallidum*. A half-century is a short period in the history of a disease which has severely plagued mankind from at least the Middle Ages. In that time, the menace of syphilis has been removed by medicine. Early elimination of the disease can be achieved only by the vigorous pursuit of the reservoirs of infection and by careful adherence to reasonable standards of social behaviour.

A NEW DRUG FOR THE TREATMENT OF ALCOHOLISM.

FOR some years much use has been made of the drug tetraethylthiuram disulphide ("Anatbuse", disulfiram) in the treatment of alcoholism. Much success has been claimed, particularly when use of the drug was combined with psychological treatment. There may, however, be very unpleasant and even dangerous symptoms after its ingestion apart from the effect of alcohol. When alcohol is taken after a dose of "Antabuse", flushing, conjunctival injection and tachycardia occur, which may later be followed by vomiting, hypotension, syncope and coma. "Antabuse" is a sulphur compound, and one of the objections to its use is that it imparts an unpleasant odour to the breath and sweat and leaves an unpleasant taste in the mouth. An investigation to find other drugs which would have essentially the same effect as "Antabuse" has been undertaken by J. K. W. Ferguson.[4]

One substance found to have the desired properties is carbimide (cyanamide). This produces the same symptoms as "Antabuse" when alcohol is taken after its ingestion. Carbimide itself is not suitable for use as a drug, for it is too unstable, setting free ammonia in solution. Pure calcium carbimide, made acid with citric acid to pH 4 or 5, makes a stable solution. The action of both "Antabuse" and carbimide is to inhibit the enzymes which break down acetaldehyde. The first oxidation product of alcohol in the body is acetaldehyde, which normally is rapidly oxidized to carbon dioxide and water or utilized in some other metabolic activity. In the presence of the drug the acetaldehyde accumulates and is responsible for the symptoms. The action of carbimide persists for only one day, whereas that of "Antabuse" lasts three or four days. Great care must be taken that only very pure carbimide is used, for the commercial cyanamides contain very toxic impurities, including cyanides.

J. D. Armstrong and Hugh T. Kerr[4] treated nineteen patients suffering from chronic alcoholism with citrated calcium carbimide (CCC). None of the patients showed any unpleasant symptoms after taking CCC; in particular there was no drowsiness, nausea, unpleasant taste or impotence, which several of the patients had complained of when taking "Antabuse".

R. G. Bell[5] has given the drug to 64 patients. He, too, found no unpleasant side effects. His conclusions after four months' continuous use of CCC are: (i) It is less toxic than "Antabuse" and is much better tolerated by the patient. This is important in that it makes it more likely that the patient will continue to use the drug for a sufficient length of time. (ii) The protection afforded by CCC is almost instantaneous. (iii) It is more rapidly eliminated from the body than "Antabuse". The uses of citrated calcium carbimide appear to be the same as those of "Antabuse" without the unpleasant side effects of the latter. The number of patients on whom the drug has been tried is small, but it seems unlikely that the new drug will have any bad effects not shown by "Antabuse", and the indications for its use are the same as those for "Antabuse". Institutional treatment is still necessary until it can be shown that it can be used outside without harm.

[1] *Arch. Dermat.*, May, 1956.
[2] *Canad. M. A. J.*, May 15, 1956.
[3] *Brit. J. Vener. Dis.*, March, 1956.
[4] *Canad. M. A. J.*, May 15, 1956.

CHLORPROMAZINE IN ANÆSTHESIA.

THE most recent addition to the multiple techniques of anæsthesia is the use of the tranquillizing effect of the drugs derived from phenothiazine, of which the most widely known at the present time is chlorpromazine hydrochloride. The ways in which chlorpromazine and allied drugs act are still not understood. One of the earliest suggestions for the use of chlorpromazine in anæsthesia concerned the considerable problems to be overcome in the new techniques of surgical operations after the induction of hypothermia. J. W. Dundee, P. R. Mesham and W. E. B. Scott,[2] on the basis of animal experiments, suggest that chlorpromazine possesses the ability to produce vasodilatation and to inhibit shivering. They found it to be the most effective of the drugs investigated in aiding the production of hypothermia. J. H. Burn[4] found that chlorpromazine prolonged the action of d-tubocurarine and itself appeared to cause some loss of excitatory capacity in skeletal muscle. Chlorpromazine also prolonged the action of barbiturates, but did not potentiate the action of morphine. C. A. Foster *et alii*[6] showed that chlorpromazine produced vasodilatation in the skin and reduced the response of the blood vessels in the hand to the cold constrictor test. Nor-epinephrine caused reversal of these changes.

Favourable results from the use of chlorpromazine as a premedicant to general anæsthesia were reported by A. B. Dobkin *et alii*[6] who found that patients were less apprehensive, less excited and talkative and less euphoric than with conventional premedicants. Induction of anæsthesia and endotracheal intubation were facilitated. Less of the anæsthetic agent was required, regardless of the type used, and there were fewer post-operative complications. The value of chlorpromazine in the prevention of post-anæsthetic vomiting was also confirmed by S. N. Albert and C. S. Coakley.[7] The addition of 50 milligrammes of chlorpromazine to the premedicants reduced the incidence of post-anæsthetic vomiting from 28·8% of a control series to 13%.

[1] *Canad. M. A. J.*, May, 1956.
[2] *Ibid.*
[3] *Anæsthesia*, October, 1954.
[4] *Proc. Roy. Soc. Med.*, August, 1954.
[5] *Lancet*, September 25, 1954.
[6] *Anæsthesia*, July, 1954.
[7] *Anæsth. & Analg.*, July-August, 1954.

D. A. B. Hopkin[1] has attempted to explain the actions of chlorpromazine, which was the combination of twenty years of French research directed towards the discovery of a drug which would either prevent or modify the effects following irritation of sympathetic nerves. An understanding, or rather an explanation, of the effects of chlorpromazine hinges considerably on the acceptance of the phenomena of the response to irritation described by J. Reilly *et alii*[2] in which the non-specific reactions to the perisplanchnic injections of all kinds of irritants were hæmorrhagic or lymphatic lesions in the organ served by the irritated nerve. Reilly and P. Tournier[3] have produced visceral and cerebral lesions by the injection of irritants into any mucosa rich in autonomic nerve fibres, particularly the pharyngeal mucosa. However, H. Selye[4] has attached more importance to the endocrine functions of the pituitary and adrenal glands, following the reaction of alarm, which occurs after the irritation.

The search for a drug which would give protection against splanchnic irritation led to the identification of chlorpromazine. Recent work has tended to show that the effects of chlorpromazine in countering the syndrome of irritation are central in origin. It now appears that chlorpromazine reduces the response of the pituitary and adrenal glands to stress. As Hopkin explains, the use of chlorpromazine as an anæsthetic premedicant induces a temporary medical hypophysectomy, an effect similar to that of promethazine. Chlorpromazine depresses most living cells, so that the narcobiotic action on nerve cells is to effect a reduction in the ability of the cell to receive and to transmit impulses. The reticular formations, made up of numerous nerve cells with short axons, must be particularly susceptible to this effect, so that the reactions to alarm are limited or lost or modified, while the cortical motor and sensory cells are much less affected. It is now seen that chlorpromazine itself has some of the actions of a selective central anæsthetic, but without the production of anæsthesia.

These views of the French workers on the physiology of the sympathetic nerves and the effects of irritation have not been received with general conviction. The so-called phenomenon of Reilly has fallen particularly under criticism, and such an authority as S. Wright[5] suggests that the explanations are so much at variance with current physiological thought, that judgement cannot be made until the whole of the experimental work has been repeated and confirmed by other reputable workers.

Despite differences on the theoretical attitudes towards the use and action of phenothiazine derivatives, the practical applications and investigations of the use of chlorpromazine hydrochloride in anæsthesia continue. J. T. Russell[6] has used chlorpromazine as an aid to general anæsthesia in 360 surgical operations of all kinds, with the exception of patients in whom the production of peripheral vasodilatation was contraindicated. The patients were each given 100 milligrammes of chlorpromazine by mouth on the evening before operation, and patients were warned to beware of subsequent dizziness on getting out of bed. Two hours before the operation a further 50 milligrammes of chlorpromazine were given by the intramuscular route. For children and small adults the dosage was one milligramme per three pounds of body weight. Atropine (one one-hundredth of a grain) was given half an hour before the operation, as the drying effect of chlorpromazine was found to be insufficient. Before operation, the patients were calm and did not appear to be apprehensive; they slept easily and lightly. The patient's skin was warm and dry and there was considerable variation in the development of pallor. There was usually a slight fall in the temperature and in the levels of blood pressure. Induction was performed uneventfully with small doses of thiopentone, and less anæsthetic than usual was required to maintain general anæsthesia. Russell notes that one of the most striking features was the failure of the patient to react adversely to shock-producing surgical procedures. Pulse and blood pressure remained stable. Similarly there was a tendency for the patient to react very little to the accumulation of carbon dioxide, so that great care was needed to avoid this situation. Operations on the head and neck were facilitated by the hypotension produced when the head was raised. No difficulties were experienced in assessing the depth of anæsthesia, and it is the author's impression that such operations as thoracotomy and cardiotomy gave less cause for anxiety when chlorpromazine was used as a premedicant. Recovery from the anæsthesia was rapid, and post-operative vomiting and nausea were minimal. No case of liver damage occurred.

Russell has had experience with the so-called "lytic cocktail", in which promethazine, chlorpromazine and pethidine are given in dilute solution by the intravenous route, but he suggests that the disadvantages of this procedure outweigh the advantages. Chlorpromazine alone has all the advantages of the "cocktail" and less of the disadvantages. Russell points out that the important feature to be observed when chlorpromazine is used is that of the extremely careful replacement of blood loss. Care is needed because of the anæsthetic effects of chlorpromazine, and with these safeguards the use of the drugs as premedicants appears to offer real advantage to the average patient in the anxious pre-operative period of waiting, in the induction and maintenance of general anæsthesia, and in the immediate post-operative recovery.

[1] *Lancet*, March 19, 1955.
[2] *Biol. Paris*, 116: 24, 1934; quoted by Hopkin, *loc. cit.*
[3] *Bull. Soc. méd. Hôp. Paris*, 70: 467, 1954; quoted by Hopkin, *loc. cit.*
[4] *Presse méd.*, April 12, 1952; quoted by Hopkin, *loc. cit.*
[5] *Lancet*, April 2, 1955.
[6] *South African M. J.*, June 9, 1956.

BILE AS A WONDER MEDICINE.

AT the Third International Congress of Internal Medicine held in Stockholm in September, 1954, Najib-Farah, an Egyptian, gave a long paper entitled "Fresh Ox Bile Percutaneously Administered as a Natural and Specific Therapeutic Agent in Rheumatic and Other Affections". The author claims that his researches over the past seventeen years have shown that bilirubinæmia is a natural defensive factor in infections and rheumatism. Prior to this paper he has published 14 papers on various aspects of the subject, many in reputable medical journals. In this paper he discusses the use of an ointment containing 50% of fresh ox bile for application to the skin for the treatment of an amazing variety of diseases. The ointment is well rubbed into the skin and the author claims that "this method of bile administration proved in my hands to be an adequate and effective therapeutic agent, suppressive and preventive, against inflammatory conditions including those of a rheumatic nature, even in cases where other methods of treatment had failed completely".

A table is given showing the results of treating 596 patients with 39 different diseases including rheumatism, gout, rheumatoid arthritis, common cold, tonsillitis, pharyngitis, bronchitis, pneumonia, acne, psoriasis, warts, impetigo, wound infections, erysipelas and even *herpes zoster*. In most cases he claims 100% recovery, except in some chronic conditions in which the recovery rate was 40% to 80%. The more acute the inflammation, the quicker the cure.

For spectacular recovery from the common cold, inunction of the ointment over the nose, forehead and cheeks for five minutes is said to cause rapid remission and cure after two to four inunctions. The author writes of this treatment for a cold: "I may state with confidence that a new era has begun in the control of this disease and sequelæ, as well as of other inflammatory affections." The author seems to be quite sincere in his claims, and he quotes a letter from a Professor A. Gigon, of the University of Basle, as stating: "I have until now six cases of arthritis which really have well responded to your bile preparation." Has the author really discovered something of importance or is this a very pronounced case of self-deception? At least the preparation and use of the ointment are simple enough.

Abstracts from Medical Literature.

MEDICINE.

Polycythæmia and Obesity.

M. H. WEIL (*J.A.M.A.*, December 24, 1955) reports four patients with polycythæmia among 260 obese patients. The incidence of polycythæmia in obese patients was found to be ten times that in the general population. Hyperplasia of the bone marrow was not observed and there was no increase in the numbers of immature cells, white cells or platelets in the peripheral blood. Splenomegaly did not occur, but functional hepatic and renal disorders were demonstrated. Arterial oxygen saturation was low, and, in an addendum, the author attributes the polycythæmia to inadequate pulmonary ventilation.

The Ætiology of Gastric and Duodenal Ulcer.

L. R. DRAGSTEDT (*Am. J. Roentgenol.*, February, 1956) states that most peptic ulcers are not due to a local decrease in resistance to digestion, although this factor may be of importance in a few cases. If local resistance was the usual determining factor, local resection of ulcers would be a more successful operation than experience has shown it to be. On the other side of the equation, the evidence is more satisfactory and favours the concept that peptic ulcers are usually due to an abnormal increase in the corrosive and digestive properties of the gastric content as a result of hypersecretion of gastric juice. There is also evidence that duodenal ulcers are usually due to a hypersecretion of gastric juice of nervous origin and that gastric ulcers are usually due to a hypersecretion of humoral or hormonal origin. The author believes that the key to the ulcer problem was provided with the discovery that the pure secretion of the fundus of the stomach has the capacity to digest all living tissue including the mucosa of the duodenum and stomach itself. Previous injury is not required, but if this is present, the damaged area succumbs more readily than the neighbouring mucosa. The disappearance of the hypersecretion in duodenal ulcer patients following complete division of the vagus nerves to the stomach indicates that the hypersecretion is of nervous origin. These widely confirmed observations provide objective evidence in support of the concept that duodenal ulcer is a psychosomatic disease. It is interesting to speculate that in some way the tensions and strain of modern life produce a secretory hypertonus in the vagus nerves and that it is in this way that the central nervous system plays a role in the disease. The persistence of hypersecretion in duodenal ulcer patients during sleep, and even after the administration of sedative drugs, suggests that the hyperactivity has become established in some of the lower ganglia. If this is true, the possibility of affecting this hypersecretion by psychotherapy seems rather remote, although the author suggests that an attempt should be made. Division of one vagus nerve does not reduce the fasting secretion which may continue even if both main trunks of the vagus supply to the stomach have been divided and provided that a relatively small branch has been left undisturbed. The fact that such a small vagus branch can activate the entire glandular mechanism of the stomach indicates that the connexion between the vagus endings and the gastric glands is not simple and direct. At all events the necessity for division of all, or nearly all, of the vagus branches to the stomach is well established; there is no doubt that many failures in the surgical treatment of duodenal ulcer have been due to incomplete vagotomy. In the early experience with gastro-enterostomy, a high incidence of marginal ulceration was encountered when this operation was performed for duodenal ulcer, but rarely when done for gastric ulcer. These observations are in harmony with the view that gastric ulcers are usually due to a hypersecretion from stasis of food in the antrum and that this is corrected by the gastro-enterostomy. In duodenal ulcer patients the hypersecretion is of nervous origin, persists after the gastro-enterostomy, and causes a new ulcer in the less resistant jejunum.

Cellular Infiltration of the Tunica Adventitia of Coronary Arteries.

L. M. GERLIS (*Brit. Heart J.*, April, 1956), in an attempt "to establish some correlation between the histological features of the coronary arteries and the mode of dying" in coronary disease, examined the coronary arteries of 101 persons who died of coronary disease, and 59 persons who died from some other cause. He paid particular attention to changes in the adventitious coat. He remarks that because atheroma is primarily a disease of the inner coats, the lesions of the outer coat have received scanty recognition. He names a number of workers who have mentioned the adventitious lesions, and goes on to describe these lesions. They consist of discrete foci of small round cells which appear to be identical with lymphocytes. They are arranged in the form of a collar round the *vasa vasorum* of the larger coronary arteries. Early lesions consist of small groups of cells adjacent to the *vasa vasorum*. Lesions of longer standing are elliptical or crescentic when seen in transverse section. In some cases numerous foci become confluent so as to encircle the coronary artery. The foci were not noted in relation to the small arteries in the myocardium. They were found in 80% of the 101 cases of death from coronary disease, and in 29% of the 59 cases of death from other causes. There appeared to be no correlation with age or sex. The lesions were found in persons aged from thirty-three to ninety-one years. The author suggests that the lesions are due to anoxia. He does not agree that they are part of the atheromatous process. He suggests that "local anoxia occurs in the fatal coronary cases as a result of spasm of the vessels, particularly the small vessels of the coronary adventitia". As the cells of the lesions appear to be of intravascular origin, it is probable that the infiltration is preceded by paralytic dilatation, which has followed the spasm. If this is correct, he states that many of the apparently sudden deaths from coronary disease "are really the terminal phase of silent 'anginal attacks' which may have been present for a considerable time, possibly several hours".

Febrile Illness After Mitral Valvotomy.

C. PAPP AND M. M. ZION (*Brit. Heart J.*, April, 1956) discuss the illness known as "postcommissurotomy syndrome" or "P.C.S.". They point out that frequently after operation on the mitral valve and removal of the auricular appendage, the patient becomes affected with fever and with sternal pain radiating to the left hemithorax. In most cases the illness commences abruptly days or weeks after the operation. The duration is from ten days to four weeks. Relapses are frequent. Several opinions have been expressed regarding the ætiology. Some authorities have suggested that it is rheumatic fever reactivated by surgical trauma. McAllister suspected a low grade infection of the lingula. Dressler considered that the illness was due to pericarditis, pleurisy and pneumonia; he compared it with idiopathic recurrent pericarditis; he suggested a rheumatic cause for both. Elster, Wood and Seely regard the illness as a self-limited form of pericarditis and pleuritis caused by surgical trauma. The authors have made a study of twenty-two patients suffering from "P.C.S.". In 14 cases the illness commenced shortly after operation (five to eleven days), in eight cases it commenced at an interval varying from four weeks to four months after operation. Relapse occurred in four cases. In the first group of patients the illness lasted from eight to thirty-four days; in the second group from four to fourteen days. The illness was not severe and the prognosis was good. Treatment generally was not effective. The authors were not impressed with the effect of aspirin or of other salicylates, except in one patient who had pains in the joints. They quote a number of points of difference between rheumatic fever and "P.C.S.". As a result of their clinical observations and study by means of X rays and electrocardiography, they conclude that the illness is due to local trauma, with post-operative hæmorrhage and loculus formation as the main causative factors. Pericarditis was revealed by electrocardiographic changes and the presence of a pleural friction rub. Left pleural effusion occurred in all cases. The authors express the opinion that "P.C.S." is the "accentuation, persistence, and recurrence of the normal post-operative sequelæ".

The Tuberculosis-Healing Factor in Cod-Liver Oil.

H. R. GETZ (*Am. Rev. Tuberc.*, April, 1956) has found that neither natural nor synthetic vitamin *A* seems to be the tuberculosis-healing factor in experimental tuberculosis. An oil with a high content of vitamin *A* (halibut-liver oil), an oil with a high content of vitamins *A* and *D* (tuna-liver oil), and a low potency cod-liver oil were used, and only the cod-liver oil showed the healing action.

A molecular distilled vitamin *A* from cod-liver oil and an oil rich in vitamin A_2 (burbot-liver oil) were used, and both failed to demonstrate the healing action. The tuberculosis-healing factor in cod-liver oil can be concentrated by saponifying the oil. The factor is found in the non-saponifiable residue along with vitamins *A* and *D*, sterols, hydrocarbons and other unknown substances.

Metastatic Cancer in the Lung.

C. R. KELLY AND H. T. LANGSTON (*J. Thoracic Surg.*, March, 1956) point out that the presence of pulmonary metastases should not be considered necessarily indicative of a fatal outcome. The surgical excision of metastatic tumours from the lung has been shown to be technically feasible and productive of a significant group of long-term survivors in selected cases. They report their experience of 18 cases, and also four other cases of tumours of the lung, thought to be metastatic, which proved to be primary.

Coarctation of the Aorta.

D. M. RING AND F. J. LEWIS (*J. Thoracic Surg.*, June, 1956) describe a syndrome in patients, particularly male patients who are no longer young, who have undergone surgical correction of coarctation of the aorta. The syndrome consists of severe abdominal pain (or distress) and tenderness, with leucocytosis and fever during the few days after the operation. Abdominal distension, rigidity, gastric dilatation or vomiting may occur. There is a tendency to spontaneous recovery; but infarction of the intestine may occur, and necrotizing arteritis and *periarteritis nodosa* may be found within the abdomen. The syndrome is attributed to over-distension of arteries lacking in resilience.

Spontaneous Remission of High Blood Pressure.

H. A. SCHROEDER AND H. M. PERRY (*Am. Heart J.*, May, 1956) found that in 247 patients admitted to hospital for the treatment of severe, sustained and prolonged hypertension, the blood pressure became and remained normal before treatment was begun. The authors advise a screening procedure as part of the evaluation of potent antihypertensive drugs, so that such patients may be excluded.

Bullous Emphysema.

H. E. WALKUP AND M. W. WOLCOTT (*Dis. Chest*, December, 1955) state that bullous emphysema becomes a clinical entity when patients with chronic hypertrophic emphysema, of a localized or generalized form, develop air cysts that are demonstrable radiographically. They consider that the treatment of choice is the local excision of the larger space-occupying bullæ. Relief of symptoms is to be looked for rather than cure; but of 14 patients treated surgically, all but one were improved, and some with a severe degree of incapacity were restored to a useful life.

The Heart and Biliary Tract Surgery.

D. MENDELSOHN AND R. MONHEIT (*New England J. Med.*, February 16, 1956) have made electrocardiographic studies of patients both during and after surgical operations on the biliary tract. There were 20 patients with no sign of heart disease, and 30 patients with signs of atherosclerotic or hypertensive heart disease or of both. Of the normal patients, six had gradual electrocardiographic changes that could not be ascribed to any particular surgical manœuvre, such as manipulation of the gall-bladder. Twenty-two of the 30 patients with abnormal hearts developed these changes. Of nine patients whose pre-operative electrocardiograms showed ischæmia, four suffered myocardial infarction. Some of the infarctions were unsuspected, and the authors conclude that closer electrocardiographic scrutiny of cardiac patients after operation is essential.

Two Kinds of Renal Hypertension.

T. FINDLEY (*Am. J. M. Sc.*, February, 1956) believes that there are two kinds of renal hypertension. Hypertension due to the excessive secretion of a pressor substance by the kidney is probably rare. The author suggests that "hyporenalism" is a more satisfactory explanation for human and experimental forms of hypertensive vascular disease. A deficit of renal tubular mass or function probably elicits a response from the anterior pituitary-adrenocortical axis, because bilateral nephrectomy indicates eosinophilia in the anterior pituitary lobe, because enucleation of the suprarenal glands produces hypertension only when one kidney has also been removed, and because the kidney in human hypertension deals with salt and water loads in the same manner as in Cushing's syndrome. Human hypertension, according to the author, could be due to a metabolic defect in the renal tubular epithelium, which renders it insensitive to trophic influences of anterior pituitary or adrenocortical origin.

Prednisone and Prednisolone in Systemic Lupus Erythematosus.

A. J. BOLLET, S. SEGA AND J. J. BUNIM (*J.A.M.A.*, December 17, 1955) have treated ten patients with systemic *lupus erythematosus* with the newer synthetic corticoids. All the patients except one had previously been incompletely controlled with cortisone, hydrocortisone and ACTH. The effect of the newer treatments on the usual manifestations of the disease are discussed at length. After following their patients for an average period of four months using an average suppressive daily dose of 35 milligrammes of either synthetic corticoid (their effects were individually indistinguishable), they draw the following conclusions: these new drugs are capable of diminishing the fever, chills, malaise, anorexia, arthritis, rash, mucous membrane lesions, cough, pleuritic and precordial pain, chest wall tenderness, pleural and pericardial friction rubs, pulmonary râles, abdominal pain and tenderness, headache, convulsive seizures, leucopenia, elevated sedimentation rate, and C-reactive protein. Renal abnormalities, the *lupus erythematosus* phenomenon, anæmia, the nephrotic syndrome, alterations in serum albumin and globulin, enlargement of the heart, and abnormalities of the electrocardiogram and the electroencephalogram did not respond to treatment. These hormones are approximately four times as potent as cortisone and hydrocortisone, and their effects are very similar, except that the new steroids do not cause sodium and water retention or potassium loss when administered in moderate therapeutic doses.

Fluorocortisone Acetate.

G. J. HAMWI AND R. F. GOLDBERG (*J.A.M.A.*, December 24, 1955) report on the use of 9α-fluorohydrocortisone in a number of clinical conditions. They find it has a cortisone-like effect averaging 15 to 20 times that of hydrocortisone in its ability to (i) inhibit the pituitary stimulation of the adrenal cortices; (ii) produce loss of nitrogen, calcium and phosphorus; (iii) inhibit inflammation; and (iv) produce a sense of well-being. Fluorocortisone acetate is five times as potent as desoxycorticosterone in promoting sodium, chloride and water retention, and potassium diuresis. Its greatest clinical usefulness will probably be in adrenal replacement therapy. It will also be valuable in those cases of acute adrenal insufficiency in which treatment must necessarily precede diagnostic study.

Urinary Excretion of 17-Ketosteroids in Normal and Undernourished Subjects.

M. RAMACHANDRAN, P. S. VENKATACHALAM AND C. GOPALAN (*Indian J.M. Res.*, April, 1956) have investigated the excretion of 17-ketosteroids in nine normal male adults, 12 normal children, six male adults with nutritional œdema, and five children aged from three to twelve years, suffering from the nutritional œdema syndrome (kwashiorkor). They point out, in the first place, that the urinary excretion of 17-ketosteroids in the normal subjects was lower than in the reported figures for English and American subjects. The urinary excretion of 17-ketosteroids, in the case of the patients suffering from nutritional œdema, was much lower than in the case of normal subjects, both children and adults. On correction of the nutritional deficiency, the excretion of 17-ketosteroids rose slowly in the adult cases, but was still below normal after forty-five to ninety days of treatment. In the children, treatment brought about a rapid return of the excretion of 17-ketosteroids to a normal level.

Steatorrhœa in Kwashiorkor.

G. MEHTA, P. S. VENKATACHALAM AND C. GOPALON (*Indian J.M. Res.*, April, 1956) have made a study of the fæcal excretion of fat in six cases of nutritional œdema syndrome in children aged from eighteen months to thirty-two months. They found that the output of fat exceeded the intake. The administration of glucose aggravated the steatorrhœa. Folic acid had no beneficial effect. Wheat diet made no difference to the steatorrhœa. Steatorrhœa was found to be more pronounced on a diet containing peanut oil than on a diet containing an equal amount of butter fat. Steatorrhœa persisted long after the patients had been clinically cured.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held on April 21, 1956, at the Ballarat and District Base Hospital. The meeting took the form of a series of clinical demonstrations by the honorary medical staff of the hospital.

Neck Stiffness.

DR. I. C. GOY (Ballarat) discussed neck stiffness. He said that it was a sign of great importance in clinical medicine. It should be sought for particularly in any case of pyrexia in childhood, and should not be neglected in the routine examination of adults. The sign itself was best described as the inability to place the chin on the chest (with the exception of cases of disease of the vertebræ), and in the extreme case neck retraction and opisthotonos occurred. Neck stiffness was best elicited with the patient lying flat on his back; the examiner with one hand behind the neck attempted to flex it passively until the chin touched the chest, a manœuvre which was prevented by spasm of the posterior cervical muscles if neck rigidity was present. In children it was often advisable to have the hand under the pillow in the manœuvre and lift head and pillow combined; that helped to eliminate voluntary resistance on the part of the child. Usually the further indications of meningeal irritation could be sought by seeing whether the child could kiss his knee, and Amos's tripod sign was well known. Kernig's sign was elicited by extending the leg with the hip flexed; that was resisted by spasm of the hamstrings provoked by downward traction of the inflamed *cauda equina*. Brudzinki's neck sign was a tonic reflex consisting of flexion of the legs when the neck was passively stretched.

Dr. Goy went on to say that the causes of neck stiffness were numerous, and in the majority of cases its presence indicated a serious disease, belonging to one of two groups: (i) acute pyogenic meningitis due to a meningococcus, a pneumococcus, *Hæmophilus influenzæ*, a hæmolytic streptococcus or a staphylococcus; (ii) acute lymphocytic meningitis—poliomyelitis, lymphocytic choriomeningitis or benign lymphocytic meningitis, mumps meningoencephalitis, infectious mononucleosis (glandular fever), leptospirosis, acute syphilitic meningitis, acute meningoencephalitis, post-infectious and otherwise (acute tuberculous meningitis). Other causes of neck stiffness were local infections in the neck, tonsillitis, sinusitis, otitis with cervical adenitis, apical pneumonia, tetanus, subarachnoid hæmorrhage, cerebral tumours (usually in the posterior fossa, in association with a high cerebro-spinal fluid pressure), cerebral abscess and "meningismus". Acute infection elsewhere might cause neck rigidity without any change in cerebro-spinal fluid except increased pressure, due to temporary over-production of cerebro-spinal fluid consequent on a reduction of the osmotic tension of the blood.

Dr. Goy then illustrated the varieties of causes of neck stiffness by briefly mentioning the cases of that type dealt with in the hospital over a period of four weeks. The patients admitted to hospital with neck stiffness had the following conditions: encephalitis, meningococcal meningitis, lymphocytic choriomeningitis, poliomyelitis, cerebral tumour, sinusitis (the patient had previously had a recurrence of meningitis from frontal sinusitis), meningismus, doubtful hysteria or malingering, pansinusitis, sunstroke, and subarachnoid hæmorrhage. He showed the patients suffering from meningococcal meningitis and poliomyelitis.

Dr. Goy said, in conclusion, that his brief review of patients admitted to the hospital with neck stiffness over a period of four weeks showed the extraordinary variety of conditions which might present with neck stiffness. It was important always to eliminate the more important causes of neck stiffness before assuming that it was one of the more mundane types.

DR. ROBERT SOUTHBY (Melbourne) pointed out the importance of sinusitis and of enlarged neck glands and occipital glands in early rubella in the differential diagnosis. He considered that in meningococcal meningitis the duration of therapy should be judged on the general improvement of the patient. He also stressed the danger of giving pertussis vaccine when poliomyelitis was active.

PROFESSOR R. R. H. LOVELL (Melbourne) pointed out how often "sunstroke" in the tropics was really missed cerebral malaria, and how service experience had disposed of old ideas on "sunstroke".

DR. A. J. WALTERS (Bendigo) suggested that much so-called "sunstroke" was in reality heat stroke and dehydration.

DR. M. S. BENSON (Geelong) spoke of his experience of heat stroke, but said that he had never seen sunstroke. He stressed the importance of convulsions in pertussis as being due to anoxia or encephalitis.

Rhabdomyosarcoma of the Myocardium.

DR. P. BANTING (Ballarat) described the case of a male child, aged twenty-one months, who had first attended his surgery on February 14, 1955, when his mother said that he had been unwell for one week. He had been listless, drowsy and irritable and looked pale; he was refusing solids, but had been very thirsty. He had had a slight cough for a few weeks. His past history had been without incident.

On examination of the patient, he was a well-nourished little boy of normal development. Some nasal congestion was present, and the only positive findings were enlarged, reddened tonsils and enlarged tonsillar glands. A diagnosis of tonsillitis was made, and he was sent home to bed, to be treated with nose drops and "Sulphatriad" tablets.

On February 16 Dr. Banting was called to see the boy at home, because he had been dry retching the previous night and had been irritable and wakeful, and was now refusing liquids.

Dr. Banting decided that the illness was probably a virus infection with associated gastritis, and with some difficulty persuaded the mother to allow him to admit the child to hospital. On his admission the patient had a temperature of 99·4° F., and he was left overnight with a rectal drip administration of fluid. On the following morning his colour had improved, but he still had a tendency to retch.

On examination of the patient his temperature was 100° F. There was still some reddening of his fauces, and there appeared to be a mass under his right costal margin. A plain X-ray examination of the abdomen was made and quickly followed by a radiological examination of the chest, the report being: "Enormous enlargement of heart shadow. The difference in shape it shows in supine and upright films would suggest that it is due to a pericardial effusion."

It was now decided that the child had pericarditis or alternatively virus myocarditis. The following morning his pallor had increased, his jugular venous pressure was raised 0·5 inch, he had *pulsus paradoxicus*, and an impalpable apex beat with a flat, dull percussion note over most of the left side of the chest. It was now certain that the abdominal mass was due to enlargement of the liver, which was palpable three fingers' breadth below the right costal margin. The electrocardiogram showed low voltage, which was present with effusion or myocarditis.

On the following morning the child's jugular venous pressure had increased to one inch and he had developed slight ankle œdema. He was transferred to the Royal Children's Hospital, where a pericardial tap was performed and 10 to 15 cubic centimetres of blood-stained fluid were withdrawn. The diagnosis of idiopathic myocarditis was made. The patient died on February 28.

The autopsy, which was performed by Dr. A. L. Williams, revealed the presence of a large tumour within the pericardial sac, almost obscuring the cardiac outline. The tumour was lobulated, and consisted of white, apparently homogeneous tissue. The main tumour mass appeared to arise from the heart in the region of the great vessels. As well as that large tumour, several small nodules of white tissue were present beneath the visceral layer of pericardium, and also in the parietal layer of pericardium. The pericardial sac also contained a considerable quanity of serosanguinous fluid. The lungs were somewhat collapsed owing to pressure from the distended pericardium, and in the upper lobe of the left lung, towards the hilum, an irregular, firm area of white tissue was present. The preliminary diagnosis was sarcoma of the heart with secondary spread to the left lung, death being due to cardiac failure. The histological appearances of the tumours were a little surprising, and the interpretation had caused Dr. Williams some concern. The large cardiac tumour and the smaller ones attached to the heart were composed of cells, the majority of which were spindle-shaped with oval nuclei. A considerable variation in size and shape of both nuclei and cells was present. A moderately large number of mitotic figures were to be seen, and the tumour had to be regarded as a sarcoma of indeterminate nature (the pleomorphism suggested origin from muscle). The secondary deposit in the lung, however, consisted of well-differentiated myocardial fibres. The difference between primary and secondary tumours was considerable, but the logical course seemed to be to regard the primary tumour as a rhabdomyosarcoma of the heart.

DR. D. A. ALEXANDER (Ballarat) discussed the difficulties of differential diagnosis between pericardial effusion and failure of a large heart.

DR. ROBERT SOUTHBY (Melbourne) suggested that the sudden death in the case under discussion might have been associated with a throat infection.

DR. D. H. MEYERS (Melbourne) discussed the use in doubtful cases of pericardial biopsy by a limited surgical incision.

Thiamine Deficiency in Heart Disease.

DR. D. A. ALEXANDER (Ballarat) discussed thiamine deficiency in heart disease. He said that Wenckebach had described the cardio-vascular signs of Oriental beriberi after observing the disease in Java in 1929-1930. The disease was advanced in the cases described, and the signs suggested for diagnosis were gross, and included (*a*) an abnormally rapid circulation time, (*b*) "pistol shot" sounds over peripheral arteries, and (*c*) a prominent right ventricle. Emphasis upon those signs had delayed the recognition of occidental beriberi.

In 1945 Marion Blankenhorn had revised the current knowledge of the effects of thiamine deficiency on the heart, and described eight requirements for the diagnosis of occidental beriberi. They were: (i) a history of dietary deficiency for at least three months, (ii) an enlarged heart with sinus rhythm, (iii) a raised jugular venous pressure, (iv) non-specific electrocardiographic changes, (v) dependent œdema, (vi) absence of other causes of heart failure, (vii) polyneuritis or pellagra, (viii) a response to specific treatment or autopsy findings consistent with beriberi.

Occidental beriberi, diagnosed on the basis of those criteria, was by no means rare as an uncomplicated disease, and certainly occurred more frequently still as an aggravating factor in other forms of heart disease.

Dr. Alexander then presented the histories of three patients with heart disease treated at the hospital since the beginning of the year, in whose condition thiamine deficiency might have been an ætiological factor.

The first patient was a postman, aged fifty-eight years, with no living relatives, who had lived in a small hotel for the past six years. He never ate breakfast, frequently missed lunch, and sometimes avoided an evening meal. A careful analysis of his diet had not been possible because of very considerable inconsistencies in his statements. His average alcohol intake exceeded 12 beers per day, with "more at the week-ends". During the first week in March, 1956, he became unduly short of breath when riding his bicycle. His legs became swollen, and he reported to the hospital on March 10.

On his admission to hospital, the following signs were noted. His blood pressure was 170 millimetres of mercury, systolic, and 90 millimetres, diastolic. The jugular venous pressure was four centimetres above normal. The heart was enlarged, with regular rhythm, and protodiastolic triple cadence. Œdema was present in his legs. The tendon reflexes were absent from the legs. Appreciation of vibration was greatly diminished in the legs. An electrocardiographic examination on March 12 revealed non-specific *T* wave changes. An X-ray examination of the chest on March 13 revealed a large heart and congested lungs. The serum albumin content was 3·6 grammes *per centum*, and the serum globulin content was 2·9 grammes *per centum*.

He was treated with thiamine hydrochloride, 50 milligrammes being given intramuscularly per day. On the eleventh day after treatment had begun, his weight had decreased by 14 pounds, his œdema had disappeared, and an X-ray film of his chest showed a normal-sized heart with normal lung fields. On the thirty-second day he felt perfectly well; his blood pressure was 120 millimetres of mercury, systolic, and 60 millimetres, diastolic, and his electrocardiogram was normal, but his vibration sense was virtually unchanged and his tendon reflexes were still absent. Dr. Alexander commented that the patient's illness fulfilled all the diagnostic requirements for beriberi heart disease described by Blankenhorn.

Dr. Alexander's second patient was a City Council foreman, aged forty-nine years, who had a normal appetite, and a diet which on analysis was adequate in proteins, minerals and vitamins. He took alcohol in moderation, rarely more than one or two beers each day. In 1954 examination showed that his blood pressure was 190 millimetres of mercury, systolic, and 120 millimetres, diastolic. On December 19, 1955, he stepped into a hole three feet deep, landed on his feet, and noticed no ill effects apart from an unpleasant jolt. Two weeks later he complained of pains in both feet and in the lower parts of his legs. X-ray examination excluded bone injury. Dr. Alexander had first examined him one week later, when he complained of constant pain from his knees to his toes. There was no objective evidence of abnormality. It was thought that his symptoms were exaggerated for the purposes of compensation. During the next two weeks the pain became worse, and extended up the legs to the hips.

Examination of the patient on February 3, 1956, revealed unusually firm, tense, swollen calf muscles, sluggish reflexes, absence of vibration sense, normal appreciation of pin-prick, and muscle power about normal. On February 6 no tendon reflexes could be elicited, and the patient was admitted to hospital for lumbar puncture. That procedure was not carried out because of the presence of a large amount of œdema over the sacrum extending up to the rib margins. There was no increase in jugular venous pressure. His blood pressure was 150 millimetres of mercury, systolic, and 90 millimetres, diastolic. The heart sounds were regular and clear, and the heart size was uncertain on clinical examination. An X-ray examination of the chest on February 9 revealed gross cardiac enlargement, but no abnormality in the lungs. An electrocardiographic examination on February 16 revealed minor changes only, with low *T* waves over the right ventricular surface leads.

The patient was treated with thiamine hydrochloride, 100 milligrammes per day given intramuscularly. Diuresis commenced in twenty-four hours. At the end of one week he was free from œdema, and his weight loss was six pounds. At the end of two weeks the transverse diameter of his heart in the radiograph had decreased by more than one inch. Clinically, at the time of the meeting, his cardiovascular system was in the same condition as it was in before the commencement of his illness, his blood pressure having returned to 160 millimetres of mercury, systolic, and 120 millimetres, diastolic. His neurological signs were improving more slowly. He was now free from paræsthesiæ, but tendon reflexes were absent in the legs. His temperature throughout his illness did not exceed 99° F.

The third of Dr. Alexander's patients, a married woman, aged fifty-four years, was a barmaid, who had been a known alcoholic for at least three years. During this time her meals had been irregular. In September, 1952, she complained of attacks of breathlessness and weakness, and the following findings were recorded. Examination of her tongue revealed atrophy of papillæ. The jugular venous pressure was slightly above normal. The blood pressure was 140 millimetres of mercury, systolic, and 100 millimetres, diastolic, with *pulsus alternans* between 140 and 120 millimetres of mercury, systolic. The heart was enlarged on clinical examination, with protodiastolic triple rhythm. Smooth, firm enlargement of the liver was palpable three inches below the costal margin. Slight œdema of the ankles was present. The ankle jerks were present, but greatly diminished by comparison with the knee jerks. Appreciation of vibration was impaired below the knees, and the patient had tingling sensations in the hands and feet. An X-ray examination of the chest revealed a greatly enlarged heart.

The patient was treated with vitamins administered parenterally, with improvement, but it was not possible to watch her progress closely.

In 1954 she had a further episode of failure, which was treated in the usual way; after that she severed her connexion with hotels and began eating normal meals. She then began having severe anginal pain with exertion, and the electrocardiogram was probably indicative of extensive coronary artery disease. She died suddenly from myocardial infarction in February, 1956. Dr. Alexander said that it was interesting that an X-ray examination shortly before her death showed the smallest heart shadow of the series.

In commenting on the cases, Dr. Alexander said that clearly only one of them could be accepted without question as typical thiamine deficiency heart disease. The second patient had a disease the nature of which was uncertain. There seemed to have been no failure of ingestion or excessive loss of thiamine, and his apparent response to thiamine administration might have been fortuitous. Possibly he had some form of polyneuritis other than that due to thiamine deficiency (for example, infective polyneuritis), and the myocardial involvement which sometimes accompanied that disorder. It was unfortunate that the lumbar puncture originally contemplated was never carried out. The studies on the third patient had not been controlled carefully enough to allow any scientifically acceptable statement to be made regarding the role of thiamine deficiency in her illness. How-

ever, there was a reasonable possibility that thiamine deficiency was the cause of some of her cardio-vascular signs. It was cases in that category to which attention should be directed. There was no difficulty in recognizing classical beriberi. There was difficulty in recognizing thiamine deficiency as an aggravating factor in other forms of heart disease. Perhaps studies of blood pyruvate levels would enable that to be done at an early stage, when treatment might be more effective.

DR. A. J. WALTERS (Bendigo) suggested that excessive ingestion of carbohydrate produced relative thiamine deficiency.

PROFESSOR R. R. H. LOVELL (Melbourne) pointed out that diuresis so often occurred with bed rest alone in cardiac failure that it was sometimes difficult to attribute improvement to specific therapy. He advised the estimation of blood pyruvate levels in the diagnosis of beriberi.

DR. T. HURLEY (Melbourne) stressed the difficulty of obtaining adequate dietary histories from patients. He considered the estimation of the urinary excretion of thiamine over twenty-four hours to be useful, but it was a tedious procedure.

Radiotherapy and its Relationship to Surgery.

DR. R. J. GOUGH (Ballarat) discussed radiotherapy and its relationship to surgery. He said that a simple definition of radiotherapy would be the use in treatment of ionizing and particle radiations. Such radiations might be produced naturally by the uranium-radium family and thorium, or artificially induced by means of X-ray machines or radioactive isotopes. Each form of particle radiated, the main members of which were α, β and neutron particles, had its own mass and velocity; it travelled in a straight line unless it was deflected by collisions or, in the case of α and β, by an electrical or magnetic field. X and γ radiations were a wave motion and fell within the electro-magnetic spectrum. They were physically identical except for their wavelengths; but where X rays were generated in the one to two million volt range, both became similar. X and γ radiations were said to be not a continuous wave motion, the energy instead being emitted in bundles or photons, and thus being likened to machine-gun bullets. The action of those radiations was due to ionization brought about when a photon struck one or more of the orbital electrons in the atom shell—causing it to be displaced and thus altering the electrical sign of the atom. The unit of X or γ radiation was the "Röntgen" (*r*), which was defined as that amount of X or γ radiation which produced in one cubic centimetre of air at normal temperature and pressure, ions of either sign carrying electrostatic unit of charge. The *r* became difficult to measure in the multimillion volt range, and was replaced as a unit by the rep or the rad—those defining the energy absorbed.

Dr. Gough then said that to explain what happened in a cell leading to biological changes in that cell there had been many theories—for example, heat production in certain vulnerable points, which was unlikely; chemical changes causing differences in pH; interference with nucleic acid metabolism; and alteration of colloid charges. It appeared that the two last-mentioned were the most likely, particularly that relating to nucleic acid metabolism. The biological effects produced in the cell were many, and the main results were five in number. They were: (i) Immediate disintegration of the cell, often after only small doses, and due to a breaking up of the internal cell structure, the inhibition of water due to increased osmotic pressure, with resultant swelling and bursting of the cell. That effect was shown by some polymorphonuclear cells and lymphocytes in inflammatory exudates, and also by the cells of some very sensitive tumours. (ii) Effects on the cell growth mechanism. Probably owing to interference with nucleic acid metabolism, delayed or abnormal mitosis might be produced, leading to a retardation of growth or the production of non-viable cells. The cell was most vulnerable in prophase, although as a point of interest the effect of neutron bombardment had been shown to be independent of the stage of mitosis. (iii) Genetic effect. That was brought about by a gene or its chromosome being rendered non-viable, or altered, so that an alteration in the adult characteristics of the cell resulted. (iv) Cytoplasm changes due to alteration in the colloid state of the cell, damage to mitochondria or Golgi apparatus, degeneration of proteins. There might follow a differentiation effect, producing completely differentiated cells which might ultimately die out. In that way, some tumour types might be rendered sterile. (v) Humoral effect. When a tumour in one site was irradiated, tumours in other areas might be reduced in size or disappear. That effect was particularly seen on irradiation of some lymph gland groups, of the spleen, of lymphosarcoma and in myeloid leuchæmia.

Dr. Gough went on to say that radiosensitivity of a tumour depended on the following factors: (*a*) The nature of the tumour bed, a good blood supply ensuring a better result and vice versa. (*b*) The nature of the tissue. Labile tissues such as the skin were more sensitive to irradiation than stable tissues such as brain and muscle *et cetera*. (*c*) Mitotic sensitivity, a cell being more sensitive in mitosis, particularly in prophase, as had been pointed out earlier. (*d*) Development. Embryonic tissues were more sensitive than similar infantile tissues, which in turn were more sensitive than similar adult tissues. Also radiosensitivity increased with phylogenetic development—the more highly developed the species, the greater the sensitivity. From those facts it would be seen that radiotherapy might serve many purposes—for example, treatment of certain inflammations, tumour destruction or growth restraint, sterilization by irradiation of the gonads, and retardation of some developmental or acquired abnormalities such as angiomata, Eales's disease and the like.

Turning to the radiotherapeutic weapons, Dr. Gough said that they included (*a*) X rays produced by potentials ranging from a few kilovolts for the treatment of very superficial lesions up to 200 to 250 kilovolts, the conventional deep therapy, and on into the multi-million volt range, (*b*) naturally occurring radioactive elements, (*c*) radioactive isotopes, and (*d*) radiomimetic drugs such as TEM, nitrogen mustard, "Myleran" *et cetera*. The aim of radiotherapy was to obtain adequate irradiation at the point of interest without unduly high dosage on its surrounding tissue or on the skin at the site of entry or exit of the beam in the case of X rays and teleradium. Apart from X rays, radium or its emanation radon might be made up into needles or seeds for implantation; or the manufacture of treatment moulds, tubes for insertion into body cavities or large quantities of radium might be used in certain equipments to produce, like an X-ray plant, beams of radiation aimed at the body from some distance—the so-called radium bomb or teleradium. Some radioactive isotopes such as radioactive cobalt, caesium and strontium, available in greater quantity and at less cost, could replace radium in some of the roles mentioned. On the other hand, the selectivity of some organs and regions might dictate the use of radioactive isotopes introduced parenterally. Well-known examples of that form of treatment were radioactive phosphorus used in the treatment of some reticuloses, and radioactive iodine used in the treatment of thyrotoxicosis and of thyroid carcinoma in some cases. Other isotopes might be used because of some inherent quality—as, for instance, radioactive colloidal gold, an α, β and γ emitter introduced into serous cavities in cases of malignant effusion, or into periprostatic tissues or paracervical tissues for the treatment of neoplasms of those organs; in those situations, because of its large molecule, the colloidal gold was slowly absorbed or phagocytosed, so that time was allowed for it to give off most of its effective radiation at the chosen site. The limitation placed upon conventional X-ray therapy—the rapid falling off in dose with penetration in depth of the beam, so that the skin obtained the maximum dose and its tolerance limited the total tumour dose—had been largely overcome by the use of multiple parts aimed at the tumour through several different skin areas; an effective total tumour dose was built up without the exceeding of skin tolerance in any particular site. Other methods of achieving that result were the use of rotational therapy, in which the X-ray beam revolved around the patient or the patient rotated in the path of the beam, and also the use of a grid, in which a perforated lead plate was placed over that part of the patient in the path of the X-ray beam; that allowed thin pencils of radiation through the skin with areas of non-irradiated skin between; on such small areas as each pencil covered, the skin could be taken beyond the dose of tolerance for a larger area. Supervoltage X-ray plants, such as the linear accelerator at present being installed at the Peter MacCallum Clinic, produced X rays of a much shorter wavelength, with resultant greater penetration and percentage depth dose.

With regard to the relationship in treatment of radiotherapy to surgery, Dr. Gough said that in the management of non-malignant conditions requiring repeated treatments to large areas, or parenteral introduction, he thought that radiotherapy should be used only when all else had failed or was definitely contraindicated. Repeated irradiation might exceed skin tolerance leading to unsightly scarring and production of indolent ulcers, or rarely radiation-induced malignant lesions might occur. With regard to parenteral treatment in such conditions, J. S. Mitchell, of Cambridge,

in a recent text-book, had suggested that when possible, the use of radioactive isotopes should be confined in non-malignant conditions to patients aged over forty-five years, because of the dangers of late carcinogenesis. He particularly cited the use of radio-iodine in the treatment of thyrotoxicosis. However, in the case of neoplastic diseases, radiotherapy should not be looked upon as the last port of call, or something to be used only to alleviate the distress of the patient after other methods had failed. Admittedly in some conditions, such as tumours of the gastro-intestinal tract, radiotherapy had little part to play, because of the inaccessibility and relative radioresistance of these tumours. Sir Stanford Cade, who was both a surgeon and a radiotherapist, had pointed out that radiotherapy was complementary to and not competitive to surgery and medicine. It was a weapon in the armamentarium of the treatment of malignant disease. The ideal arrangement would be that described by Professor McWhirter which existed in Edinburgh, where all new patients were examined and the treatment was planned by a group consisting at least of a physician and surgeon of a particular speciality and a radiotherapist. Other centres, such as the Peter MacCallum Clinic in Melbourne, were gradually establishing such consultative planning. In most cases, it was wrong to say that surgery was the treatment of this condition or radiotherapy the treatment of that. Rather, after assessment, it should be said that one or other would be the primary form of treatment, and a policy should be drawn up for the further treatment or management of complications. A rule of thumb, but one probably open to much argument, would be that radiotherapy should become the primary treatment in cases in which it gave results equal to or better than surgery. The reason for such a decision was that radiotherapy would usually require or result in less mutilation than surgery. Cases which illustrated such a statement included the treatment of carcinoma of the tongue, palate or lip; radiotherapy in those sites gave far better cosmetic and therefore psychological results. However, the remainder of the policy should then be laid down—for example, that surgery or a radon implant should be used for local recurrence or gland metastases. Some, including R. Kaye Scott in Melbourne and Ralston Patterson in Manchester, arranged that, in the case of lip cancer, when a primary lesion was larger than half an inch in diameter, radiotherapy was followed by unilateral or bilateral dissection of cervical lymph nodes, according to the position of the primary tumour on the lip. On the other hand, in some breast tumours the opposite held; stage I and some stage II tumours were primarily treated by surgery with irradiation of the operation site, and related gland fields post-operatively, although some workers also preferred pre-operative irradiation. In some situations, as in the case of malignant ovarian tumours, operation first was inevitable, laparotomy being necessary perhaps to discover the site of the tumour, remove it and allow its nature to be determined; the type and plan of radiotherapy then depended on the pathology of the lesion. Sir Stanford Cade quoted the figures of Heymann for five-year cures in cases of stage I carcinoma of the cervix treated by irradiation. There were 58·7% of cures, so that 41% of those who were left developed recurrences, due either to resistance of some tumour cells or to inadequate therapy. He advised close follow-up of the patient with operation when the recurrence was discovered; but the present policy of the Peter MacCallum Clinic—the performance of Wertheim's hysterectomy eight weeks after the conclusion of therapy—seemed preferable. In the case of inoperable malignant disease, radiotherapy still had a large part to play in bringing about alleviation of pain, hæmorrhage and fungations and in prolonging the useful life of the patient, just as the hypertensive and cardiac patient was never actually cured of his condition, but it was palliated and he was assisted to lead a normal life.

DR. E. S. R. HUGHES (Melbourne) said that the radiotherapist must be a good clinician with enthusiasm and a knowledge of technique. Dr. Gough possessed all these attributes; but some radiotherapists lacked them, and assumed the care of patients who would be better dealt with surgically. He himself was reluctant to accept radiotherapy for more than a few conditions. He said that the surgical treatment of carcinoma of the lip was not a mutilating procedure, and that the patient with a small rodent ulcer treated by radiotherapy was not infrequently left with a large scar. Cases of *pruritus ani* were not well dealt with; a common sequence of treatment seemed to be the use of ointment, reference to a psychiatrist, and, finally, the administration of radiotherapy by a dermatologist, the net result being that the patient developed a cancerophobia, linking radiotherapy with malignant disease.

(To be continued.)

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

DIETARY SCALE AT NORFOLK ISLAND, 1793.[1]

[From the Journal of Phillip Gidley King, Lieutenant Governor.]

A CONVICT died at Queensboro after suffering inexpressible torments for 3 days. His death was occasioned by eating the whole of his week's allowance at a meal, which was followed by an indigestion or obstruction in his Stomach and notwithstanding the exertions of the Surgeon he died in great agony. Another convict from the same cause had nearly shared the same fate, but these instances are not sufficient to prevent many of those people from devouring their whole week's ration at one meal, which has obliged them to thieve or starve the remainder of the week. To remedy this inconvenience I directed the Deputy Commissioner to make two servings a week, to convicts of this description which ensures them a meal at the latter end of the week. Before this regulation took place, there were many among them that did not taste a bit of meat from Sunday till the following Saturday. As some little relief to people of this description I ordered a great part of the Fish which were caught to be given to the Surgeon who caused a large mess to be made of them with Rice Portable Soup and Vegetables and as there were three large Boars and four old sows belonging to Government I directed two of them to be killed on Fridays and boiled up in the same manner as the fish were, which has been a great relief to those who came out on the last ships who are in general so weak and emaciated that they are little better than Invalids.

The average number of sick during this month has been ninety one (in a population including women and children of 1155), among which number extreme weakness seems to be the prevailing complaint, which is confined to those objects who came out in the last ships as the same general good state of health prevails among every other description of people.

Correspondence.

THE WONDER DRUGS OF PSYCHIATRY.

SIR: Replying to Dr. Douglas Everingham (M. J. AUSTRALIA, August 25, 1956), may I explain that my initial enthusiasm about the new sedatives was so dampened by practical experience that I attempted to seek information about: (*a*) the word "ataraxic", as I said, "out of drug house Greek by the *Zeitgeist*"; (*b*) something that I may have mistaken for histological gaucherie in the psychiatrist—locating the action of these drugs "in the *formatio reticularis* above the superior *corpora quadrigemina*" (perhaps we were away the day our groups as medical students dissected the epithalamus!); and (*c*) the cost of the treatment (which has since been decided on an official level by the Federal Treasurer to be prohibitive)?

In detail, Dr. Everingham informs us that my "reckoning is awry at least as regards my postulates". I postulate nothing. As for cost, the drug houses know where I obtain my figures from all right; the printed trade cost-indices are supplied by them to all pharmacists and equally readily available to any medical man as well. The doses are from the original article in your columns ("The Use of Reserpine, Chlorpromazine and Allied Drugs in Medicine and Psychiatry", M. J. AUSTRALIA, June 23, 1956). Reserpine costs £2 3s. 6d. for 500 tablets of 0·25 milligramme; chlorpromazine £23 5s. for the same number of 100 milligramme tablets; the other "chemical tranquillizers"—for example, "Frenquil" *et cetera—cost* 1s. *each tablet; and "Caramaphen" £1* 1s. *for* 50 tablets. Patients discharged on leave from these hospitals had also been taking phenobarbitone and bromide mixture (at 9s. 6d. per week), and phenolphthalein and paraffin emulsion (not much less expensive) as well. I

[1] From the original in the Mitchell Library, Sydney.

learned these facts in the turmoil of general practice from the living experience. My submission is that at the maintenance dosage rate needed by a severe chronic psychotic, the cost of all these added up by something less fallible than a prejudiced human cerebral cortex is still "about £250,000 for the forty or fifty years that the usual asylum 'lifer' would need them".

The usual asylum "lifer" is, for example, a paraphrenic who has made a murderous or a perverted libidinous attack on somebody, appears "normal" for decades, and then repeats the performance if given the opportunity. The lunatic asylums (why not call a spade a spade?) of this country are still chock full of unfortunates who need "institutional care and treatment for their own protection or the protection of others". The buildings come to us from the pre-Florence Nightingale era where architectural emphasis is on solidity and façade rather than on nursing possibilities, sanitation and ventilation; they are not hospitals, Dr. Everingham. They are controlled by "Lunacy" Acts and are filled from "reception houses"—not from therapeutic wards for the mentally ill. They are staffed by psychiatrists who are government servants, which is to say specialists (i) in knowing the unknowable, the human mind; (ii) abject subservience to authority attained by seniority; and (iii) suppression of their own personality in public relations (for example, my own skit about them in this, the national medical publication of this country, has not been replied to by them).

Perhaps I did not succeed in expressing my amusement at the very word "ataraxic", which the literate psychiatrists of Great Britain find no different from sedatives and to be classed with alcohol and tobacco as expensive luxuries, at least until they are shown to be the "sweet oblivious antidote", to "cleanse the stuff'd bosom of that perilous stuff that weighs upon the heart" (*Macbeth*, Act V).

Modern ignorance cloaks itself in neologisms from the ancient Greek—for example, "ataraxic", "iatrogenia" (I do not thank thee, Dr. Schmalzbach, for teaching me that word—M. J. AUSTRALIA, July 14, 1956, page 84—a psychiatric note), and the very word "psychiatry" itself, which is only ten years older than Sigmund Freud and much less reputable. What evidential difference is there between ascribing mental disorder to the moon (lunacy), rather than to the reticular formation in the diencephalon (a mechanical solecism) put forward in the monograph I criticize?

In case Dr. Everingham still thinks that "psychiatric drugs" from the hands of someone who has become a specialist by wandering in the bad lands beyond science on the fringe of metaphysics while a resident in a mental hospital is the answer to the psychoses, I will give Shakespeare's answers:

> How does your patient, doctor?
> Not so sick, my lord,
> As she is troubled with thick-coming fancies
> That keep her from her rest.

and

> Canst thou not minister to a mind diseas'd;
> Pluck from the memory a rooted sorrow;
> Raze out the written troubles of the brain. . . .
> Therein the patient
> Must minister to himself.

And there my judgement of psychiatry remains in spite of the palliation that nursing, psychocatharsis, electroconvulsive therapy and sedatives provides.

Yours, etc.,

607 New South Head Road, Rose Bay, New South Wales.
August 27, 1956.

GODFREY HARRIS.

NEW SOUTH WALES STATE CANCER COUNCIL: SPECIAL UNIT FOR INVESTIGATION AND TREATMENT—ADMISSION OF PATIENTS.

SIR: In July, 1955, the New South Wales State Cancer Council accepted the principle that patients in the public and intermediate classifications should be admitted to the above unit, a principle which has received the approval of the Hospitals Commission of New South Wales. This decision followed a report by the Honorary Director that the incidence of the various types of cancer varied among the social strata of the community, and therefore the study of patients should not be restricted to any one category. It was realized that certain fees would be earned by the visiting staff, and the following decisions were reached:

1. That a special fund should be authorized by the Cancer Council to receive fees so earned by the surgeons.

2. That this fund should have as its objects: (*a*) provision of amenities for the patients and staff as approved by the Cancer Council; (*b*) publication fund to finance the proper presentation of research work; (*c*) travelling fellowships for the nursing staff.

It is obvious that in accordance with current hospital practice this decision would apply to the surgeons rather than to the anæsthetists and visiting physicians.

The actual technique by which these decisions will be implemented is now under discussion.

Yours, etc.,

B. T. EDYE.
(On behalf of the New South Wales State Cancer Council.)
"Craignish", 185 Macquarie Street, Sydney.
September 5, 1956.

CORTISONE AND ANÆSTHESIA.

SIR: Dr. Patricia Wilson (M. J. AUSTRALIA, August 25, 1956) has given us a timely reminder of the danger of operating on patients who are being treated with cortisone. Her patient with ulcerative colitis, after treatment lasting thirteen days, collapsed and died the day after operation for multiple perforations of the colon.

A second lesson can be learned from this case if we ask ourselves why perforation of the colon should have occurred. Dr. Wilson mentions peptic ulceration as one of the complications of cortisone treatment. But its effects are not confined to the stomach and duodenum; Levin *et alii* (1953) reported two deaths from perforation of the bowel in rheumatoid patients treated with steroids.

The occurrence of multiple perforations so soon after the beginning of treatment with cortisone cannot be fortuitous. There can be little doubt that the drug adversely affected the ulcerative process, either through a special effect on the alimentary tract or through its general action which favours the spread of infections. Whatever "antiallergic" activities cortisone may possess do not justify its use in colitis; they are more than offset by these two undesirable possibilities.

Yours, etc.,

34 Queens Road, Melbourne,
September 4, 1956.

MICHAEL KELLY.

Reference.

LEVIN, M. H., *et alii* (1953), "The Prolonged Treatment of Rheumatoid Arthritis with Cortisone and Corticotrophin", *Am. J. Med.*, 14: 265.

Post-Graduate Work.

THE MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

PROGRAMME FOR OCTOBER, NOVEMBER AND DECEMBER, 1956.

Country Courses.

Horsham.—At Horsham, on Saturday, October 13, the following course will be given: "Neurological Problems in General Practice", Dr. J. Billings; "Recent Advances in Pædiatrics", Dr. Mostyn Powell; "Surgery of the Gall-Bladder", Dr. E. S. R. Hughes. Dr. Ross Webster, Lister House, Horsham (telephone 103) is the local secretary for this course.

Bendigo.—At Bendigo, on Saturday, October 20, at the School of Nursing, Rowan Street, the following course will be given: 2.30 p.m., "Coronary Disease", Dr. G. A. Penington; 4 p.m., "Infertility", Dr. J. W. Johnstone; 5 p.m., "Modern Management of Diabetes", Dr. W. Hamilton Smith. Dr. A. J. Walters, 514 High Street, Golden Square, Bendigo (telephone 228), is the local secretary for this course.

Ballarat.—At Ballarat, on Thursday, October 25, at 8 p.m., at Craig's Hotel, Sir Macfarlane Burnet will speak on "The Present State of Virus Disease".

Swan Hill.—At Swan Hill, on Saturday, November 3, the following course will be given: 2 p.m., "The Management of Burns", Dr. J. C. Stewart and Dr. I. H. Cuming; 3 p.m., "The Management of Arthritis", Dr. R. Strang; 4.30 p.m., "Habitual Abortion", Dr. C. N. de Garis. The course is the one which has been postponed from August 11 and then from October 27. It will be held in the Lecture Theatre, Swan Hill High School, Pye Street, Swan Hill. Dr. R. Weaver is the local secretary. Address: 18 Beveridge Street. Telephone, Swan Hill 139.

Mooroopna.—At Mooroopna Base Hospital on Saturday, November 10, the following course will be given: 2.15 p.m., "Modern Trends in Fracture Treatment", Dr. Eric Price; 4.30 p.m., "Modern Trends in Cancer Treatment", Dr. R. Kaye Scott. Dr. B. R. Schloeffel, Maude Street, Shepparton (telephone 67), is the local secretary for this course.

Warrnambool.—At Warrnambool, on Saturday, November 17, the following two papers will be read: "Cardiac Arrhythmia", Dr. Maurice Clarke; "Bladder Neck Obstruction", Dr. J. B. Somerset. These papers will be followed by an evening lecture to the subdivision, arranged by the Royal College of Obstetricians and Gynæcologists, by Professor Andrew Claye, Professor of Gynæcology and Obstetrics, University of Leeds. Dr. W. R. Angus, 214 Koroit Street, Warrnambool (telephone 52), is the honorary secretary for this course.

Flinders Naval Depot.—At Flinders Naval Depot, at 2.30 p.m. on Wednesdays, the following courses will be given by arrangement with the Royal Australian Navy: October 10, "Diseases of the Pancreas", Dr. Ian Wood; November 14, neurosurgical subject, Dr. K. Bradley; December 5, "Difficulties in Surgery of the Biliary Tract", Dr. A. J. W. Ahern.

Overseas Lecturers.

Professor L. J. Witts, Nuffield Professor of Clinical Medicine, Radcliffe Infirmary, Oxford, will give the following lectures at the Medical Society Hall at 8.15 p.m.: Tuesday, October 9, "Modern Concepts in the Diagnosis and Treatment of Anæmia"; Tuesday, October 16, "The Relations between Anæmia and the Alimentary Tract"; Thursday, October 18, "The Present Position of the ACTH and Corticoids in Treatment". The fee is 15s. per lecture, but those who have paid an annual subscription to the committee may attend without further charge. In addition, Professor Witts will visit the teaching hospitals and attend meetings of The Royal Australasian College of Physicians.

Attention is also drawn to the lecture by Dr. W. S. Jordan, Exchange Visitor at the Royal Melbourne Hospital, from Cleveland, Ohio, where he is Assistant Professor of Preventive Medicine at the Western Reserve University. On Wednesday, October 3, at 8.15 p.m. in the Medical Society Hall, he will lecture to the medical profession on "The Study of Infectious Diseases in Families: An Experimental Survey".

Attention is also drawn to the lecture by Dr. Howard Rusk, of the Bellvue Rehabilitation Centre, New York, in the Public Lecture Theatre, University of Melbourne, on Monday, November 12, at 8 p.m. This lecture has been arranged by the Australian Section of Physical Medicine of the British Medical Association.

Inquiries.

The address of the Melbourne Medical Post-Graduate Committee is 394 Albert Street, East Melbourne. Telephone: FB 2547.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Week-End Course in Rheumatic Diseases.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that a week-end course in rheumatic diseases will be conducted at the Royal Prince Alfred Hospital from 10 a.m. to 5 p.m. on Saturday, October 20, and from 10 a.m. to 1 p.m. on Sunday, October 21, 1956. The fee for attendance will be £3 3s., and the course will be of interest to general practitioners. Further particulars may be obtained on application to the Course Secretary, Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 4497, BU 4498. Telegraphic address: "Postgrad Sydney."

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED SEPTEMBER 8, 1956.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	2(1)	6(4)	..	1	..	..	..	9
Amœbiasis	..	1	..	..	3(3)	..	..	..	4
Ancylostomiasis	..	..	1	..	..	..	..	..	1
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	2	8(7)	..	..	..	..	..	..	10
Diphtheria	1	..	..	..	..	..	..	..	1
Dysentery (Bacillary)	..	9(7)	..	..	..	..	3	..	12
Encephalitis	..	..	..	2(2)	..	..	..	..	2
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	1(1)	..	..	..	..	..	..	1
Infective Hepatitis	70(36)	37(18)	..	18(4)	2(2)	11(1)	3	2	143
Lead Poisoning	..	..	..	..	1	..	..	..	1
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	4	..	..	..	..	..	4
Malaria	..	..	1(1)	..	..	..	..	..	1
Meningococcal Infection	3(2)	4(3)	..	..	..	2	..	..	9
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1	2(2)	..	1(1)	1(1)	..	..	..	5
Puerperal Fever	1	..	1	..	..	..	..	..	2
Rubella	..	29(23)	..	4(3)	..	..	..	..	33
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	12(11)	7(6)	5(3)	2(2)	1(1)	..	..	1	28
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	1	1	..	..	..	2
Trachoma	..	..	..	..	..	..	6	..	6
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	31(25)	24(20)	24(14)	5(4)	16(12)	7(3)	..	1	108
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	1	..	..	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Australasian Medical Publishing Company, Limited.

ANNUAL MEETING.

THE adjourned annual meeting of the Australasian Medical Publishing Company, Limited, was held at The Printing House, Seamer Street, Glebe, New South Wales, on September 19, 1956, DR. W. L. CALOV, the Vice-Chairman, in the chair.

Directors' Report.

The report of the directors of the company was as follows:

The directors submit their report for the twelve months ended June 30, 1956, together with the balance sheet as at June 30, 1956, and the profit and loss account for the twelve months ended June 30, 1956.

The contributions to THE MEDICAL JOURNAL OF AUSTRALIA have been of high standard and the journal continues to increase in size and circulation. It now has a weekly circulation of over 11,000 copies.

A satisfactory result was obtained from the year's production of the printing and publishing department, and arrangements have been made for the payment of debenture interest for the year ended June 30, 1956.

During the year work commenced on the western extension to The Printing House. Early in 1956 the builders encountered extremely bad weather and completion of the building is not expected until some time in the first half of 1957.

The company's reserves are used in the business, and we consider the state of the company's affairs is satisfactory.

Sir Henry S. Newland and Dr. W. F. Simmons retire from office by rotation in accordance with the Articles of Association (Article 39). They are eligible and present themselves for reelection.

W. L. CALOV,
September 12, 1956. Vice-Chairman.

Election of Directors.

Sir Henry S. Newland and Dr. W. F. Simmons were reelected to the Board of Directors.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE following additions and amendments have been made to the Register of Medical Practitioners for New South Wales in accordance with the *Medical Practitioners Act*, 1938-1955:

Registered medical practitioner who is required to complete twelve months' hospital service in accordance with the provisions of Section 17 (3) and is registered under Section 17 (1) (*a*) of the Act: D'Assumpcao, Carlos Augusto Rocha, M.B., B.S., 1956 (Univ. Adelaide).

Registered medical practitioner who has complied with the requirements of Section 17 (3) and is registered under Section 17 (1) (*a*) of the Act: Denton, James Graham, M.B., B.S., 1954 (Univ. Adelaide).

The following medical practitioners have submitted evidence of having completed twelve months' hospital service, pursuant to the provisions of Section 17 (3) of the Act: Bowdler, John Denby; Llewellyn-Smith, Ronald Leslie; Llewellyn-Smith, Hazel May; Jamieson, Walter Connal; McClure, Peter James; Mooy, Antony; Destro, Nicholas; O'Mara, Matthew Douglas; Blanche, Paul Douglas; Morgan, John Joseph.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Llewellyn-Smith, Ronald Leslie, M.B., B.S., 1955 (Univ. Sydney), 58-60 Myrtle Street, Sydney.

Royal Australasian College of Surgeons.

OPEN MEETING.

A MEETING of the Royal Australasian College of Surgeons will be held in the Stawell Hall, 143 Macquarie Street, Sydney, on October 4, 1956, at 8.15 p.m. Dr. M. P. Susman, Dr. A. F. Grant and Dr. L. Atkinson will speak on "The Results of Treatment of Cancer of the Lung". The meeting is open to all medical practitioners.

Deaths.

THE following deaths have been announced:

MACKENZIE.—Donald Stewart MacKenzie, on August 21, 1956, at Mount Lawley, Western Australia.

STREICH.—Carl Ivo Streich, on September 1, 1956, at Perth.

STENNING.—Arthur Ernest Stenning, on September 2, 1956, at Busselton, Western Australia.

Diary for the Month.

OCT. 2.—New South Wales Branch, B.M.A.: Council Quarterly
OCT. 3.—Western Australian Branch, B.M.A.: Branch Council.
OCT. 5.—Queensland Branch, B.M.A.: General Meeting (Jackson Lecture).
OCT. 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
OCT. 9.—New South Wales Branch, B.M.A.: Organization and Science Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 *per annum* within Australia and the British Commonwealth of Nations, and £6 *per annum* within America and foreign countries, payable in advance.